

# Dossier zur Nutzenbewertung gemäß § 35a SGB V

*Trastuzumab-Deruxtecan (Enhertu®)*

Daiichi Sankyo Deutschland GmbH

## Modul 4 A

*Erwachsene Patienten mit inoperablem oder metastasiertem HER2-low Brustkrebs, die bereits eine Chemotherapie in der metastasierten Situation erhalten haben*

Medizinischer Nutzen und  
medizinischer Zusatznutzen,  
Patientengruppen mit therapeutisch  
bedeutsamem Zusatznutzen



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**Anhang 4-G 1: Ergänzende Analysen DESTINY-Breast04: Mortalität**

**Anhang 4-G 1.1: Gesamtüberleben**

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DE.T.1.1.1 - Overall survival - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	149 (39.9)	90 (48.9)	
Number of subjects censored, n (%)	224 (60.1)	94 (51.1)	
Median time to first event (months) [a]	23.4	16.8	
95% Confidence Interval	[20.0, 24.8]	[14.5, 20.0]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.6408
95% Confidence Interval			[0.4903, 0.8375]
p-value			0.0011
Stratified log-rank p-value [c]			0.0010

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.1.1.2 - Overall survival - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
HER2 status											0.7682
HER2 IHC 1+	214	81 (37.9)	133 (62.1)	24.7 (19.8, NE)	107	53 (49.5)	54 (50.5)	15.7 (13.5, 20.6)	0.6079 (0.4297, 0.8598)	0.0049	0.0045
HER2 IHC 2+ /ISH Negative	159	68 (42.8)	91 (57.2)	21.5 (18.5, 24.5)	77	37 (48.1)	40 (51.9)	16.8 (13.6, NE)	0.6409 (0.4282, 0.9591)	0.0305	0.0292

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.1.1.2 - Overall survival - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.6145
1	221	73 (33.0)	148 (67.0)	24.7 (21.7, NE)	100	45 (45.0)	55 (55.0)	17.5 (15.2, NE)	0.5868 (0.4044, 0.8516)	0.0045	
>=2	151	76 (50.3)	75 (49.7)	18.1 (16.1, 24.5)	83	45 (54.2)	38 (45.8)	14.1 (10.8, 20.2)	0.6861 (0.4739, 0.9934)	0.0447	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Prior CDK4/6											0.3376
Yes	235	101 (43.0)	134 (57.0)	20.8 (18.2, 24.5)	118	55 (46.6)	63 (53.4)	16.7 (14.1, 20.0)	0.6999 (0.5037, 0.9727) 0.0336	0.0325	
No	98	28 (28.6)	70 (71.4)	NE (NE, NE)	48	21 (43.8)	27 (56.3)	19.9 (15.6, NE)	0.5260 (0.2982, 0.9277) 0.0265	0.0240	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											0.9205
<65	290	117 (40.3)	173 (59.7)	23.4 (19.7, 24.8)	136	67 (49.3)	69 (50.7)	16.0 (14.1, 20.0)	0.6188 (0.4579, 0.8362)	0.0018	
>=65	83	32 (38.6)	51 (61.4)	23.9 (17.2, NE)	48	23 (47.9)	25 (52.1)	17.1 (11.1, NE)	0.6420 (0.3752, 1.0987)	0.1029	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Age										0.8167
<75	359	145 (40.4)	214 (59.6)	21.7 (19.8, NE)	175	86 (49.1)	89 (50.9)	16.7 (14.1, 19.9)	0.6161 (0.4715, 0.8050) 0.0004	0.0003
>=75	14	4 (28.6)	10 (71.4)	23.9 (8.2, NE)	9	4 (44.4)	5 (55.6)	23.6 (4.8, 23.6)	0.5373 (0.1197, 2.4129) 0.4176	0.4103

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.1.1.2 - Overall survival - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Race											0.9259
White	176	80 (45.5)	96 (54.5)	19.8 (17.2, 24.5)	91	47 (51.6)	44 (48.4)	14.8 (10.7, 19.5)	0.6223 (0.4335, 0.8935) 0.0102	0.0094	
Non-White	197	69 (35.0)	128 (65.0)	NE (21.5, NE)	92	43 (46.7)	49 (53.3)	17.1 (15.2, NE)	0.6106 (0.4169, 0.8945) 0.0113	0.0105	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Region											0.9557
Asia	147	51 (34.7)	96 (65.3)	NE (21.7, NE)	66	31 (47.0)	35 (53.0)	19.9 (15.7, NE)	0.6056 (0.3871, 0.9474) 0.0280	0.0265	
North America	60	27 (45.0)	33 (55.0)	19.0 (15.6, 24.7)	33	19 (57.6)	14 (42.4)	14.9 (10.5, 19.4)	0.6184 (0.3377, 1.1321) 0.1193	0.1170	
Europe + Israel	166	71 (42.8)	95 (57.2)	20.8 (18.2, 24.5)	85	40 (47.1)	45 (52.9)	15.1 (10.7, NE)	0.6584 (0.4463, 0.9712) 0.0351	0.0340	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
ECOG PS											
0	200	69 (34.5)	131 (65.5)	24.5 (20.8, NE)	105	44 (41.9)	61 (58.1)	19.4 (15.2, NE)	0.5850 (0.4006, 0.8543)	0.0055	0.7140
1	173	80 (46.2)	93 (53.8)	19.8 (17.0, 24.7)	79	46 (58.2)	33 (41.8)	14.9 (12.6, 19.5)	0.6573 (0.4560, 0.9474)	0.0234	

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 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Number of lines of endocrine therapy received in the metastatic setting											0.1476
0	60	24 (40.0)	36 (60.0)	NE (16.6, NE)	34	21 (61.8)	13 (38.2)	12.9 (8.0, 23.6)	0.5063 (0.2815, 0.9108) 0.0231	0.0206	
1	108	44 (40.7)	64 (59.3)	23.4 (17.0, NE)	51	19 (37.3)	32 (62.7)	20.2 (15.6, NE)	1.0200 (0.5952, 1.7481) 0.9425	0.9407	
2	115	41 (35.7)	74 (64.3)	23.9 (20.0, NE)	54	27 (50.0)	27 (50.0)	16.0 (10.5, 19.5)	0.4530 (0.2762, 0.7429) 0.0017	0.0013	
>=3	90	40 (44.4)	50 (55.6)	21.7 (18.1, NE)	45	23 (51.1)	22 (48.9)	16.8 (12.6, NE)	0.6078 (0.3628, 1.0183) 0.0586	0.0560	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:09; Program name: T1\_OS\_2\_FAS.sas; Output name: T1\_OS\_2\_FAS.rf

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.0834
PD	174	81 (46.6)	93 (53.4)	18.8 (16.9, 21.7)	85	36 (42.4)	49 (57.6)	19.4 (12.6, NE)	0.8778 (0.5926, 1.3003) 0.5156	0.5122	
PR	48	17 (35.4)	31 (64.6)	NE (18.2, NE)	22	13 (59.1)	9 (40.9)	15.1 (8.0, NE)	0.3859 (0.1862, 0.7997) 0.0104	0.0078	
SD	82	31 (37.8)	51 (62.2)	23.9 (19.7, NE)	55	32 (58.2)	23 (41.8)	16.8 (12.6, 20.0)	0.4978 (0.3027, 0.8187) 0.0060	0.0051	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.1.1.2 - Overall survival - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Reported history of CNS metastases											0.7005
Yes	37	20 (54.1)	17 (45.9)	19.0 (13.4, 24.8)	15	7 (46.7)	8 (53.3)	NE (5.7, NE)	0.7212 (0.2973, 1.7497) 0.4699	0.4659	
No	336	129 (38.4)	207 (61.6)	23.9 (20.1, NE)	169	83 (49.1)	86 (50.9)	16.9 (14.8, 20.0)	0.6059 (0.4596, 0.7987) 0.0004	0.0003	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.8944
Yes	24	15 (62.5)	9 (37.5)	16.7 (8.4, 24.5)	8	5 (62.5)	3 (37.5)	7.9 (0.6, NE)	0.6264 (0.2189, 1.7928)	0.3791	
No	349	134 (38.4)	215 (61.6)	23.9 (20.1, NE)	176	85 (48.3)	91 (51.7)	16.9 (14.8, 20.0)	0.6129 (0.4668, 0.8048)	0.0004	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:09; Program name: T1\_OS\_2\_FAS.sas; Output name: T1\_OS\_2\_FAS.rf

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Renal function at baseline											0.0120
Normal Function	202	78 (38.6)	124 (61.4)	21.7 (20.0, 24.7)	87	43 (49.4)	44 (50.6)	15.2 (12.6, 22.4)	0.5601 (0.3854, 0.8139) 0.0024	0.0020	
Mild Impairment	123	47 (38.2)	76 (61.8)	NE (18.2, NE)	69	35 (50.7)	34 (49.3)	15.7 (11.1, 19.4)	0.5371 (0.3458, 0.8344) 0.0057	0.0049	
Moderate Impairment	41	20 (48.8)	21 (51.2)	17.2 (13.3, NE)	23	8 (34.8)	15 (65.2)	23.6 (17.5, NE)	1.9112 (0.8381, 4.3579) 0.1235	0.1173	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.4520
Normal Function	170	50 (29.4)	120 (70.6)	NE (24.7, NE)	98	39 (39.8)	59 (60.2)	22.4 (16.9, NE)	0.6176 (0.4061, 0.9393) 0.0243	0.0229
Mild Impairment	195	93 (47.7)	102 (52.3)	19.8 (17.2, 23.9)	84	49 (58.3)	35 (41.7)	12.7 (8.2, 15.6)	0.5110 (0.3603, 0.7246) 0.0002	0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Baseline visceral disease											0.0153
Yes	332	142 (42.8)	190 (57.2)	21.7 (19.0, 24.5)	157	74 (47.1)	83 (52.9)	17.0 (14.8, 20.2)	0.6883 (0.5194, 0.9121) 0.0093	0.0088	
No	41	7 (17.1)	34 (82.9)	NE (NE, NE)	27	16 (59.3)	11 (40.7)	15.1 (12.9, 20.6)	0.2199 (0.0899, 0.5380) 0.0009	0.0003	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (IXRS)											0.3719
Positive	331	126 (38.1)	205 (61.9)	23.9 (20.8, 24.8)	163	73 (44.8)	90 (55.2)	17.5 (15.2, 22.4)	0.6519 (0.4884, 0.8703) 0.0037	0.0034	
Negative	42	23 (54.8)	19 (45.2)	16.6 (11.3, NE)	21	17 (81.0)	4 (19.0)	10.3 (6.1, 15.2)	0.5172 (0.2748, 0.9735) 0.0410	0.0385	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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DE.T.1.1.2 - Overall survival - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (derived)											0.3366
Positive	333	128 (38.4)	205 (61.6)	23.9 (20.8, 24.8)	166	76 (45.8)	90 (54.2)	17.0 (15.2, 20.2)	0.6457 (0.4858, 0.8582) 0.0026	0.0024	
Negative	40	21 (52.5)	19 (47.5)	18.2 (13.6, NE)	18	14 (77.8)	4 (22.2)	8.3 (5.6, 20.6)	0.4818 (0.2438, 0.9519) 0.0356	0.0318	

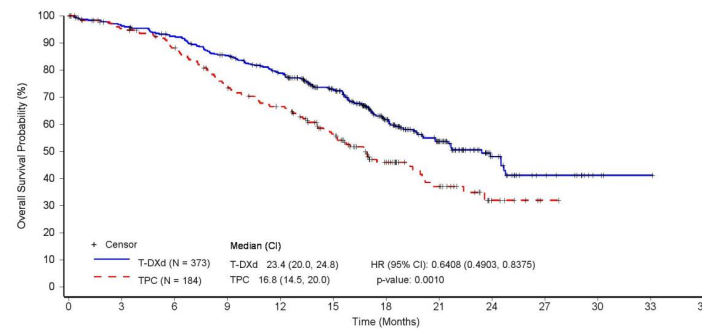
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:09; Program name: T1\_OS\_2\_FAS.sas; Output name: T1\_OS\_2\_FAS.rtf

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DE.F.1.1.3 - Overall survival - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

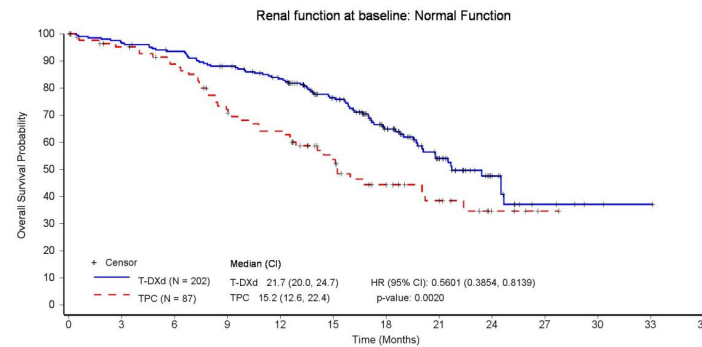
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T-DXd (N = 373)	373	357	338	309	276	214	129	78	32	12	3	1	0
TPC (N = 184)	184	161	146	120	105	77	42	25	7	1	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:08; Program name: F1\_OS\_3\_FAS.sas; Output name: F1\_OS\_3\_FAS.rf

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 DE.F.1.1.4 - Overall survival - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

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Patients still at risk:

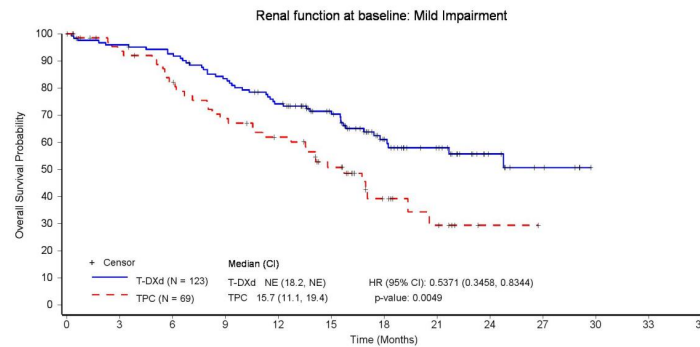
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33	36
T-DXd (N = 202)	202	195	187	174	158	121	75	42	17	5	2	1	0
TPC (N = 87)	87	77	70	55	48	32	19	13	4	1	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

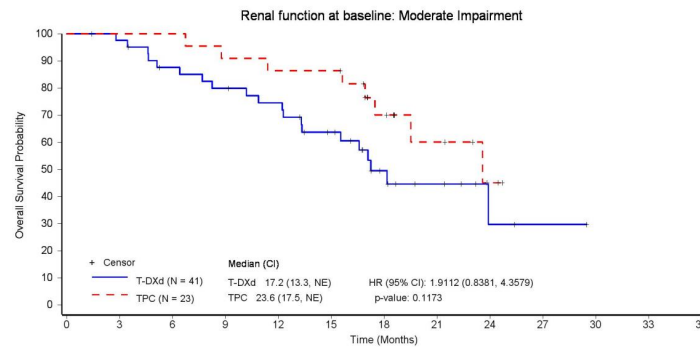
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33	36
T-DXd (N = 123)	123	117	112	100	87	69	41	29	12	5	0	0	0
TPC (N = 69)	69	58	50	41	35	25	11	6	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:08; Program name: F1\_OS\_4\_FAS.sas; Output name: F1\_OS\_4\_FAS.rf

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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33	36
T-DXd (N = 41)	41	40	34	31	28	21	10	6	2	1	0	0	0
TPC (N = 23)	23	22	22	20	19	19	11	6	2	0	0	0	0

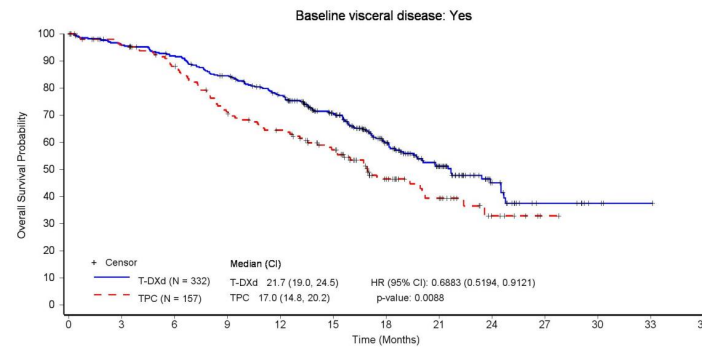
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:08; Program name: F1\_OS\_4\_FAS.sas; Output name: F1\_OS\_4\_FAS.rf



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Patients still at risk:

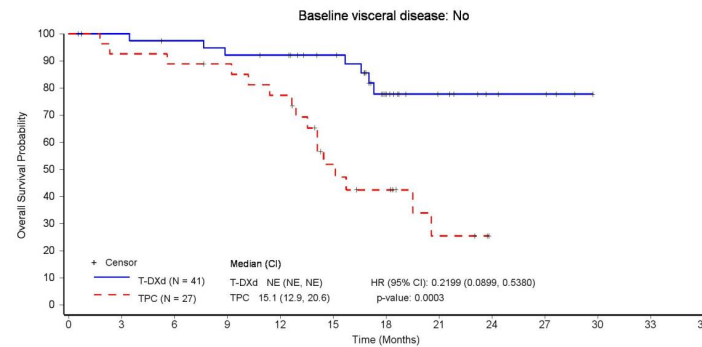
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33	36
T-DXd (N = 332)	332	318	301	274	242	185	113	69	27	8	3	1	0
TPC (N = 157)	157	136	122	97	85	66	34	22	7	1	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:08; Program name: F1\_OS\_4\_FAS.sas; Output name: F1\_OS\_4\_FAS.tf

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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33	36
T-DXd (N = 41)	41	39	37	35	34	29	16	9	5	4	0	0	0
TPC (N = 27)	27	25	24	23	20	11	8	3	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:08; Program name: F1\_OS\_4\_FAS.sas; Output name: F1\_OS\_4\_FAS.rf

**Anhang 4-G 2: Ergänzende Analysen DESTINY-Breast04: Morbidität**

**Anhang 4-G 2.1: Progressionsfreies Überleben**

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DE.T.2.1.1 - Progression-free survival based on BICR - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	243 (65.1)	127 (69.0)	
Number of subjects censored, n (%)	130 (34.9)	57 (31.0)	
Median time to first event (months) [a]	9.9	5.1	
95% Confidence Interval	[9.0, 11.3]	[4.2, 6.8]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.5014
95% Confidence Interval			[0.4013, 0.6265]
p-value			<0.0001
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:09; Program name: T1\_OS\_1\_FAS.sas; Output name: T2\_PFS\_BICR\_1\_FAS.rtf

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DE.T.2.1.2 - Progression-free survival based on BICR - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.4860
HER2 IHC 1+	214	134 (62.6)	80 (37.4)	10.0 (8.6, 12.3)	107	75 (70.1)	32 (29.9)	4.8 (3.0, 7.0)	0.4748 (0.3558, 0.6336) <0.0001	<0.0001
HER2 IHC 2+/ISH Negative	159	109 (68.6)	50 (31.4)	9.9 (8.0, 11.5)	77	52 (67.5)	25 (32.5)	5.1 (2.9, 7.1)	0.5459 (0.3901, 0.7639) 0.0004	0.0003

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 13SEP2022 – 17:09; Program name: T1\_OS\_2\_FAS.sas; Output name: T2\_PFS\_BICR\_2\_FAS.rtf

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DE.T.2.1.2 - Progression-free survival based on BICR - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.7213
1	221	141 (63.8)	80 (36.2)	10.1 (8.4, 12.2)	100	68 (68.0)	32 (32.0)	6.4 (4.3, 7.8)	0.5222 (0.3891, 0.7007)	<0.0001
>=2	151	101 (66.9)	50 (33.1)	9.7 (8.1, 11.4)	83	59 (71.1)	24 (28.9)	4.2 (3.0, 5.4)	0.4896 (0.3527, 0.6795)	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.2.1.2 - Progression-free survival based on BICR - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Prior CDK4/6											
Yes	235	151 (64.3)	84 (35.7)	10.0 (8.1, 11.3)	118	77 (65.3)	41 (34.7)	5.4 (3.0, 7.0)	0.5453 (0.4123, 0.7212) <0.0001	<0.0001	0.4001
No	98	62 (63.3)	36 (36.7)	11.5 (9.5, 16.4)	48	36 (75.0)	12 (25.0)	5.4 (4.3, 8.1)	0.4211 (0.2769, 0.6404) 0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 13SEP2022 – 17:09; Program name: T1\_OS\_2\_FAS.sas; Output name: T2\_PFS\_BICR\_2\_FAS.rtf

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DE.T.2.1.2 - Progression-free survival based on BICR - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Age										0.3765
<65	290	191 (65.9)	99 (34.1)	9.8 (8.4, 11.1)	136	93 (68.4)	43 (31.6)	4.6 (2.9, 5.9)	0.4740 (0.3681, 0.6102)	<0.0001
>=65	83	52 (62.7)	31 (37.3)	11.4 (8.3, 13.3)	48	34 (70.8)	14 (29.2)	6.2 (4.3, 10.8)	0.5683 (0.3647, 0.8854)	0.0114

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 13SEP2022 – 17:09; Program name: T1\_OS\_2\_FAS.sas; Output name: T2\_PFS\_BICR\_2\_FAS.rtf



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DE.T.2.1.2 - Progression-free survival based on BICR - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Age											
<75	359	236 (65.7)	123 (34.3)	9.9 (8.6, 11.3)	175	121 (69.1)	54 (30.9)	4.6 (4.0, 6.2)	0.4797 (0.3835, 0.6001) <0.0001	<0.0001	0.1958
>=75	14	7 (50.0)	7 (50.0)	11.5 (2.9, NE)	9	6 (66.7)	3 (33.3)	12.6 (2.5, NE)	1.0737 (0.3544, 3.2525) 0.9000	0.8998	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 13SEP2022 – 17:09; Program name: T1\_OS\_2\_FAS.sas; Output name: T2\_PFS\_BICR\_2\_FAS.rtf

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Race										0.0886
White	176	116 (65.9)	60 (34.1)	9.7 (8.4, 11.5)	91	54 (59.3)	37 (40.7)	5.6 (3.1, 8.3)	0.6300 (0.4541, 0.8739) 0.0057	0.0053
Non-White	197	127 (64.5)	70 (35.5)	10.3 (8.3, 12.2)	92	72 (78.3)	20 (21.7)	4.8 (3.0, 6.2)	0.4281 (0.3184, 0.5755) <0.0001	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Region										0.1364
Asia	147	94 (63.9)	53 (36.1)	10.9 (9.0, 13.8)	66	53 (80.3)	13 (19.7)	4.6 (2.8, 6.4)	0.3778 (0.2672, 0.5341) <0.0001	<0.0001
North America	60	46 (76.7)	14 (23.3)	8.0 (4.2, 10.0)	33	20 (60.6)	13 (39.4)	4.5 (2.9, 7.2)	0.6207 (0.3599, 1.0704)	0.0836
Europe + Israel	166	103 (62.0)	63 (38.0)	10.3 (8.5, 12.3)	85	54 (63.5)	31 (36.5)	6.9 (2.9, 8.4)	0.0863 0.6027 (0.4321, 0.8407) 0.0029	0.0026

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:09; Program name: T1\_OS\_2\_FAS.sas; Output name: T2\_PFS\_BICR\_2\_FAS.rtf

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	200	127 (63.5)	73 (36.5)	10.9 (9.5, 12.0)	105	64 (61.0)	41 (39.0)	5.8 (3.0, 8.2)	0.5157 (0.3797, 0.7003) <0.0001	<0.0001	0.7434
1	173	116 (67.1)	57 (32.9)	9.6 (7.1, 11.3)	79	63 (79.7)	16 (20.3)	4.8 (4.0, 5.9)	0.4948 (0.3620, 0.6764) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting										0.0151
0	60	41 (68.3)	19 (31.7)	9.5 (5.7, 12.2)	34	27 (79.4)	7 (20.6)	4.0 (1.4, 5.1)	0.3990 (0.2427, 0.6559)	0.0002
1	108	77 (71.3)	31 (28.7)	8.5 (6.9, 9.9)	51	32 (62.7)	19 (37.3)	7.8 (4.2, 10.7)	0.7962 (0.5257, 1.2058)	0.2777
2	115	64 (55.7)	51 (44.3)	12.0 (9.9, 15.1)	54	39 (72.2)	15 (27.8)	4.5 (2.9, 5.9)	0.3125 (0.2056, 0.4750)	<0.0001
>=3	90	61 (67.8)	29 (32.2)	10.3 (7.5, 13.3)	45	29 (64.4)	16 (35.6)	5.4 (2.7, 11.0)	0.5964 (0.3795, 0.9371)	0.0238

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.2298
PD	174	123 (70.7)	51 (29.3)	8.6 (7.2, 9.9)	85	57 (67.1)	28 (32.9)	4.6 (2.9, 6.2)	0.5381 (0.3912, 0.7402) 0.0001	0.0001
PR	48	33 (68.8)	15 (31.3)	11.4 (7.1, 13.8)	22	17 (77.3)	5 (22.7)	2.8 (1.4, 4.8)	0.2775 (0.1511, 0.5096) <0.0001	<0.0001
SD	82	47 (57.3)	35 (42.7)	12.0 (8.4, 19.2)	55	40 (72.7)	15 (27.3)	8.1 (4.4, 10.7)	0.5021 (0.3253, 0.7751) 0.0019	0.0015

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.2.1.2 - Progression-free survival based on BICR - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.7077
Yes	37	30 (81.1)	7 (18.9)	8.1 (5.4, 10.0)	15	10 (66.7)	5 (33.3)	2.0 (1.2, 11.0)	0.5777 (0.2791, 1.1956) 0.1393	0.1345
No	336	213 (63.4)	123 (36.6)	10.3 (9.5, 11.7)	169	117 (69.2)	52 (30.8)	5.3 (4.2, 6.9)	0.4915 (0.3906, 0.6186) <0.0001	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.4228
Yes	24	18 (75.0)	6 (25.0)	8.1 (4.0, 11.3)	8	6 (75.0)	2 (25.0)	4.8 (0.6, 11.0)	0.7063 (0.2777, 1.7962)	0.4634
No	349	225 (64.5)	124 (35.5)	10.1 (9.5, 11.5)	176	121 (68.8)	55 (31.3)	5.1 (4.2, 6.8)	0.4937 (0.3941, 0.6184)	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Renal function at baseline											0.1510
Normal Function	202	137 (67.8)	65 (32.2)	10.0 (9.0, 11.3)	87	63 (72.4)	24 (27.6)	4.2 (2.8, 5.4)	0.4181 (0.3077, 0.5681) <0.0001	<0.0001	
Mild Impairment	123	79 (64.2)	44 (35.8)	8.6 (7.0, 12.6)	69	46 (66.7)	23 (33.3)	6.2 (3.1, 8.3)	0.5080 (0.3502, 0.7369) 0.0004	0.0003	
Moderate Impairment	41	22 (53.7)	19 (46.3)	12.2 (6.0, NE)	23	14 (60.9)	9 (39.1)	7.2 (4.5, NE)	0.8857 (0.4526, 1.7333) 0.7231	0.7122	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:09; Program name: T1\_OS\_2\_FAS.sas; Output name: T2\_PFS\_BICR\_2\_FAS.rtf

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DE.T.2.1.2 - Progression-free survival based on BICR - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.7466
Normal Function	170	99 (58.2)	71 (41.8)	12.0 (9.7, 16.4)	98	68 (69.4)	30 (30.6)	5.4 (4.3, 8.1)	0.4623 (0.3379, 0.6326) <0.0001	<0.0001
Mild Impairment	195	137 (70.3)	58 (29.7)	9.6 (7.3, 10.8)	84	57 (67.9)	27 (32.1)	4.3 (2.8, 6.9)	0.5011 (0.3648, 0.6882) <0.0001	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.2.1.2 - Progression-free survival based on BICR - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline visceral disease										0.0437
Yes	332	223 (67.2)	109 (32.8)	9.7 (8.4, 10.8)	157	110 (70.1)	47 (29.9)	5.4 (4.2, 7.0)	0.5470 (0.4339, 0.6897)	<0.0001
No	41	20 (48.8)	21 (51.2)	17.9 (11.3, 26.4)	27	17 (63.0)	10 (37.0)	3.0 (1.6, 12.4)	0.2567 (0.1280, 0.5146)	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Hormon receptor status (IXRS)											
Positive	331	211 (63.7)	120 (36.3)	10.1 (9.5, 11.5)	163	110 (67.5)	53 (32.5)	5.4 (4.4, 7.1)	0.5093 (0.4028, 0.6439) <0.0001	<0.0001	0.5491
Negative	42	32 (76.2)	10 (23.8)	6.6 (4.1, 11.7)	21	17 (81.0)	4 (19.0)	2.9 (1.4, 4.0)	0.4473 (0.2424, 0.8257) 0.0101	0.0083	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Run date: 13SEP2022 – 17:09; Program name: T1\_OS\_2\_FAS.sas; Output name: T2\_PFS\_BICR\_2\_FAS.rtf

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Hormon receptor status (derived)											
Positive	333	213 (64.0)	120 (36.0)	10.1 (9.5, 11.5)	166	113 (68.1)	53 (31.9)	5.4 (4.3, 7.0)	0.5053 (0.4006, 0.6374) <0.0001	<0.0001	0.6872
Negative	40	30 (75.0)	10 (25.0)	8.5 (4.3, 11.7)	18	14 (77.8)	4 (22.2)	2.9 (1.4, 5.1)	0.4595 (0.2380, 0.8873) 0.0205	0.0177	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

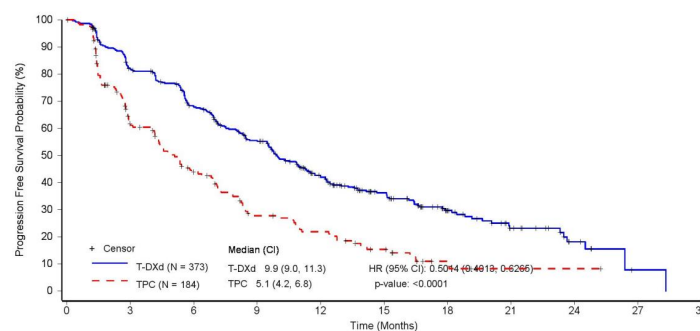
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Run date: 13SEP2022 – 17:09; Program name: T1\_OS\_2\_FAS.sas; Output name: T2\_PFS\_BICR\_2\_FAS.rtf

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Patients still at risk:

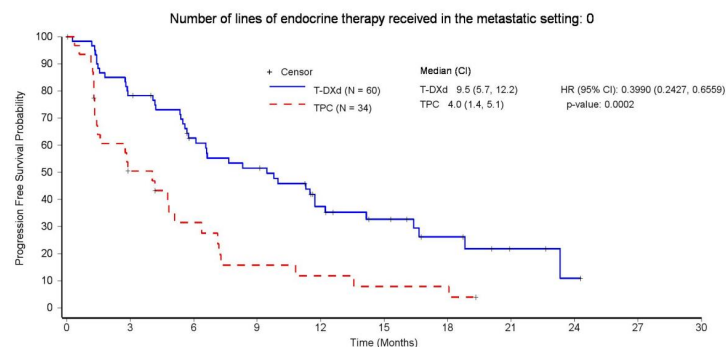
	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 373)	373	295	238	183	118	81	42	21	8	1	0
TPC (N = 184)	184	93	60	34	26	13	4	1	1	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:08; Program name: F1\_OS\_3\_FAS.sas; Output name: F2\_PFS\_BICR\_3\_FAS.rf

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Patients still at risk:

T-DXd (N = 60)	60	47	34	28	17	12	7	3	1	0	0
TPC (N = 34)	34	14	8	4	3	2	2	0	0	0	0

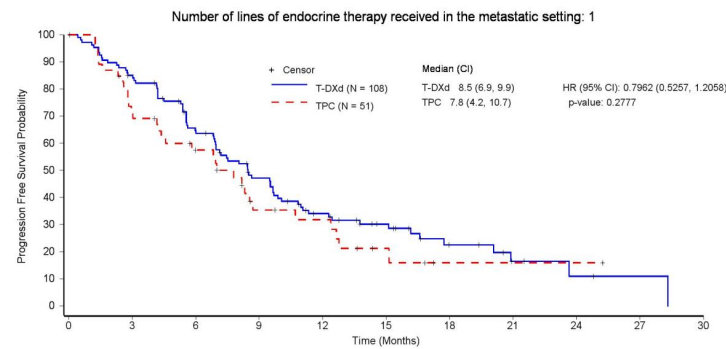
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:09; Program name: F1\_OS\_4\_FAS.sas; Output name: F2\_PFS\_BICR\_4\_FAS.rf

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DE.F.2.1.4 - Progression-free survival based on BICR - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

T-DXd (N = 108)	108	90	65	44	28	19	9	4	2	1	0
TPC (N = 51)	51	32	23	11	9	4	1	1	1	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

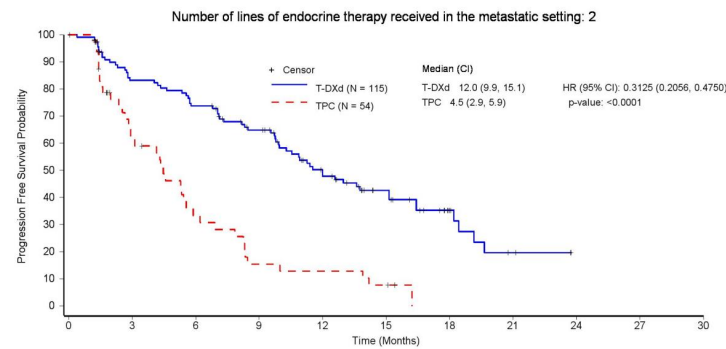
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 Run date: 21OCT2022 – 18:09; Program name: F1\_OS\_4\_FAS.sas; Output name: F2\_PFS\_BICR\_4\_FAS.rf



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DE.F.2.1.4 - Progression-free survival based on BICR - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 115)	115	88	78	63	40	25	11	3	0	0	0
TPC (N = 54)	54	25	13	6	5	3	0	0	0	0	0

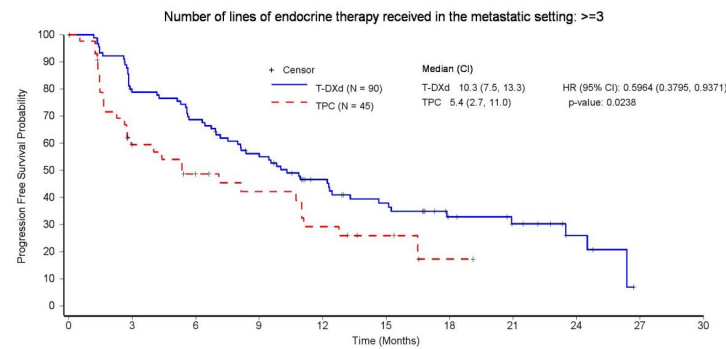
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:09; Program name: F1\_OS\_4\_FAS.sas; Output name: F2\_PFS\_BICR\_4\_FAS.rf

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DE.F.2.1.4 - Progression-free survival based on BICR - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

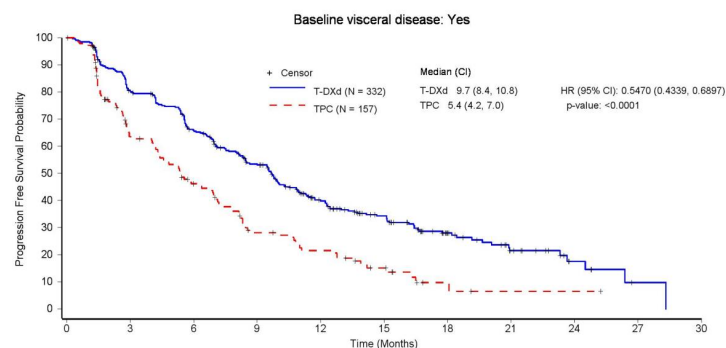
	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 90)	90	70	61	48	33	25	15	11	5	0	0
TPC (N = 45)	45	22	16	13	9	4	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:09; Program name: F1\_OS\_4\_FAS.sas; Output name: F2\_PFS\_BICR\_4\_FAS.rf

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Patients still at risk:

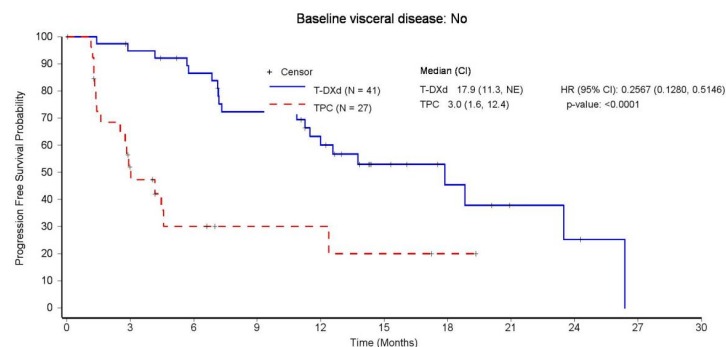
	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 332)	332	259	207	158	99	71	36	18	6	1	0
TPC (N = 157)	157	82	55	31	23	11	3	1	1	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:09; Program name: F1\_OS\_4\_FAS.sas; Output name: F2\_PFS\_BICR\_4\_FAS.rf

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Patients still at risk:

T-DXd (N = 41)	41	36	31	25	19	10	6	3	2	0	0
TPC (N = 27)	27	11	5	3	3	2	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:09; Program name: F1\_OS\_4\_FAS.sas; Output name: F2\_PFS\_BICR\_4\_FAS.rf

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DE.T.2.2.1 - Progression-free survival based on investigator's assessment - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	270 (72.4)	151 (82.1)	
Number of subjects censored, n (%)	103 (27.6)	33 (17.9)	
Median time to first event (months) [a]	8.8	4.2	
95% Confidence Interval	[8.3, 9.8]	[3.0, 4.5]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.3672
95% Confidence Interval			[0.2967, 0.4545]
p-value			<0.0001
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 13SEP2022 – 17:10; Program name: T1\_OS\_1\_FAS.sas; Output name: T2\_PFS\_INVE\_1\_FAS.rtf

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DE.T.2.2.2 - Progression-free survival based on investigator's assessment - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.4829
HER2 IHC 1+	214	150 (70.1)	64 (29.9)	9.6 (8.1, 10.0)	107	88 (82.2)	19 (17.8)	4.2 (3.0, 5.3)	0.3495 (0.2650, 0.4611) <0.0001	<0.0001
HER2 IHC 2+/ISH Negative	159	120 (75.5)	39 (24.5)	8.5 (7.5, 10.0)	77	63 (81.8)	14 (18.2)	4.0 (2.8, 4.6)	0.3946 (0.2879, 0.5409) <0.0001	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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DE.T.2.2.2 - Progression-free survival based on investigator's assessment - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.5593
1	221	155 (70.1)	66 (29.9)	9.6 (8.4, 10.9)	100	82 (82.0)	18 (18.0)	4.3 (3.0, 5.4)	0.3913 (0.2966, 0.5163) <0.0001	<0.0001
>=2	151	114 (75.5)	37 (24.5)	8.3 (6.9, 9.7)	83	69 (83.1)	14 (16.9)	3.8 (2.7, 4.5)	0.3499 (0.2559, 0.4783) <0.0001	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Prior CDK4/6											
Yes	235	173 (73.6)	62 (26.4)	8.3 (7.2, 9.5)	118	96 (81.4)	22 (18.6)	4.2 (2.9, 4.6)	0.3891 (0.2999, 0.5048) <0.0001	<0.0001	0.6845
No	98	62 (63.3)	36 (36.7)	11.3 (9.8, 13.4)	48	39 (81.3)	9 (18.8)	5.4 (2.8, 7.6)	0.3244 (0.2147, 0.4902) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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DE.T.2.2.2 - Progression-free survival based on investigator's assessment - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Age											
<65	290	213 (73.4)	77 (26.6)	9.1 (8.2, 9.8)	136	110 (80.9)	26 (19.1)	3.8 (2.8, 4.5)	0.3525 (0.2772, 0.4482) <0.0001	<0.0001	0.4065
>=65	83	57 (68.7)	26 (31.3)	8.8 (7.0, 12.0)	48	41 (85.4)	7 (14.6)	5.0 (4.0, 7.0)	0.4103 (0.2699, 0.6236) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 13SEP2022 – 17:10; Program name: T1\_OS\_2\_FAS.sas; Output name: T2\_PFS\_INVE\_2\_FAS.rtf

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Age											
<75	359	262 (73.0)	97 (27.0)	8.8 (8.3, 9.8)	175	143 (81.7)	32 (18.3)	4.1 (2.9, 4.5)	0.3558 (0.2875, 0.4403) <0.0001	<0.0001	0.2892
>=75	14	8 (57.1)	6 (42.9)	8.8 (5.6, NE)	9	8 (88.9)	1 (11.1)	9.4 (2.5, 13.6)	0.6329 (0.2360, 1.6973) 0.3634	0.3594	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 13SEP2022 – 17:10; Program name: T1\_OS\_2\_FAS.sas; Output name: T2\_PFS\_INVE\_2\_FAS.rtf

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Race										0.5442
White	176	131 (74.4)	45 (25.6)	8.5 (7.5, 9.8)	91	69 (75.8)	22 (24.2)	4.0 (2.8, 4.9)	0.4122 (0.3039, 0.5591) <0.0001	<0.0001
Non-White	197	139 (70.6)	58 (29.4)	9.5 (8.2, 10.9)	92	81 (88.0)	11 (12.0)	4.2 (2.9, 5.4)	0.3430 (0.2583, 0.4555) <0.0001	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Region										0.4836
Asia	147	104 (70.7)	43 (29.3)	9.8 (8.3, 11.2)	66	59 (89.4)	7 (10.6)	4.2 (2.7, 5.4)	0.3198 (0.2299, 0.4448) <0.0001	<0.0001
North America	60	44 (73.3)	16 (26.7)	8.5 (5.6, 11.0)	33	25 (75.8)	8 (24.2)	3.8 (1.8, 4.6)	0.3106 (0.1786, 0.5401) <0.0001	<0.0001
Europe + Israel	166	122 (73.5)	44 (26.5)	8.4 (7.1, 9.5)	85	67 (78.8)	18 (21.2)	4.2 (2.9, 5.3)	0.4436 (0.3260, 0.6036) <0.0001	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	200	135 (67.5)	65 (32.5)	9.8 (8.8, 11.1)	105	80 (76.2)	25 (23.8)	4.1 (2.8, 4.9)	0.3433 (0.2578, 0.4573) <0.0001	<0.0001	0.4007
1	173	135 (78.0)	38 (22.0)	7.9 (6.9, 8.5)	79	71 (89.9)	8 (10.1)	4.2 (2.9, 5.0)	0.4016 (0.2973, 0.5426) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting										0.0077
0	60	45 (75.0)	15 (25.0)	7.0 (5.6, 10.0)	34	30 (88.2)	4 (11.8)	2.9 (1.4, 4.2)	0.3467 (0.2138, 0.5622) <0.0001	<0.0001
1	108	83 (76.9)	25 (23.1)	8.4 (7.1, 9.7)	51	37 (72.5)	14 (27.5)	5.6 (4.2, 7.0)	0.6219 (0.4191, 0.9229) 0.0184	0.0170
2	115	74 (64.3)	41 (35.7)	9.9 (8.4, 11.2)	54	45 (83.3)	9 (16.7)	4.2 (2.9, 5.0)	0.2585 (0.1720, 0.3884) <0.0001	<0.0001
>=3	90	68 (75.6)	22 (24.4)	9.6 (7.3, 11.3)	45	39 (86.7)	6 (13.3)	2.8 (2.3, 4.4)	0.3021 (0.1999, 0.4566) <0.0001	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.3516
PD	174	136 (78.2)	38 (21.8)	8.3 (6.9, 8.5)	85	68 (80.0)	17 (20.0)	3.4 (2.8, 4.3)	0.3656 (0.2689, 0.4972)	<0.0001
PR	48	37 (77.1)	11 (22.9)	9.7 (7.6, 13.8)	22	20 (90.9)	2 (9.1)	3.4 (1.8, 5.4)	0.1935 (0.1044, 0.3588)	<0.0001
SD	82	54 (65.9)	28 (34.1)	11.0 (7.2, 12.6)	55	46 (83.6)	9 (16.4)	5.1 (4.0, 5.8)	0.4195 (0.2802, 0.6281)	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.9633
Yes	37	33 (89.2)	4 (10.8)	7.9 (5.5, 10.6)	15	13 (86.7)	2 (13.3)	2.2 (1.2, 4.5)	0.3955 (0.2023, 0.7730) 0.0067	0.0051
No	336	237 (70.5)	99 (29.5)	9.3 (8.3, 9.9)	169	138 (81.7)	31 (18.3)	4.2 (3.4, 4.9)	0.3637 (0.2923, 0.4525) <0.0001	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.2.2.2 - Progression-free survival based on investigator's assessment - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.3455
Yes	24	20 (83.3)	4 (16.7)	8.5 (4.2, 11.3)	8	7 (87.5)	1 (12.5)	3.6 (0.6, 8.3)	0.5429 (0.2237, 1.3175)	0.1716
No	349	250 (71.6)	99 (28.4)	9.1 (8.3, 9.8)	176	144 (81.8)	32 (18.2)	4.2 (3.0, 4.5)	0.3603 (0.2910, 0.4462)	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Renal function at baseline											0.1728
Normal Function	202	149 (73.8)	53 (26.2)	8.4 (7.5, 9.8)	87	76 (87.4)	11 (12.6)	3.8 (2.7, 4.5)	0.3259 (0.2437, 0.4358) <0.0001	<0.0001	
Mild Impairment	123	89 (72.4)	34 (27.6)	9.6 (8.0, 11.0)	69	51 (73.9)	18 (26.1)	4.1 (2.8, 5.0)	0.3211 (0.2226, 0.4632) <0.0001	<0.0001	
Moderate Impairment	41	27 (65.9)	14 (34.1)	10.0 (6.6, 14.4)	23	20 (87.0)	3 (13.0)	7.2 (4.0, 9.7)	0.5773 (0.3214, 1.0369) 0.0660	0.0628	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.9354
Normal Function	170	119 (70.0)	51 (30.0)	10.9 (9.1, 12.3)	98	77 (78.6)	21 (21.4)	4.4 (4.0, 5.7)	0.3354 (0.2486, 0.4525) <0.0001	<0.0001
Mild Impairment	195	144 (73.8)	51 (26.2)	7.9 (6.9, 8.8)	84	72 (85.7)	12 (14.3)	3.9 (2.6, 4.5)	0.3755 (0.2799, 0.5039) <0.0001	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline visceral disease										0.0021
Yes	332	248 (74.7)	84 (25.3)	8.5 (8.1, 9.7)	157	129 (82.2)	28 (17.8)	4.2 (3.1, 5.0)	0.4129 (0.3314, 0.5144) <0.0001	<0.0001
No	41	22 (53.7)	19 (46.3)	12.4 (8.8, 24.9)	27	22 (81.5)	5 (18.5)	2.9 (1.4, 4.5)	0.1337 (0.0668, 0.2674) <0.0001	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.2.2.2 - Progression-free survival based on investigator's assessment - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (IXRS)										0.6257
Positive	331	233 (70.4)	98 (29.6)	9.6 (8.4, 10.0)	163	132 (81.0)	31 (19.0)	4.2 (3.4, 4.9)	0.3721 (0.2983, 0.4643) <0.0001	<0.0001
Negative	42	37 (88.1)	5 (11.9)	5.7 (4.2, 8.5)	21	19 (90.5)	2 (9.5)	2.9 (1.5, 4.2)	0.3200 (0.1718, 0.5959) 0.0003	0.0002

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Hormon receptor status (derived)											
Positive	333	235 (70.6)	98 (29.4)	9.5 (8.4, 10.0)	166	135 (81.3)	31 (18.7)	4.2 (3.8, 4.9)	0.3707 (0.2976, 0.4618) <0.0001	<0.0001	0.5071
Negative	40	35 (87.5)	5 (12.5)	6.3 (4.2, 8.5)	18	16 (88.9)	2 (11.1)	2.9 (1.4, 4.2)	0.2929 (0.1510, 0.5680) 0.0003	0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

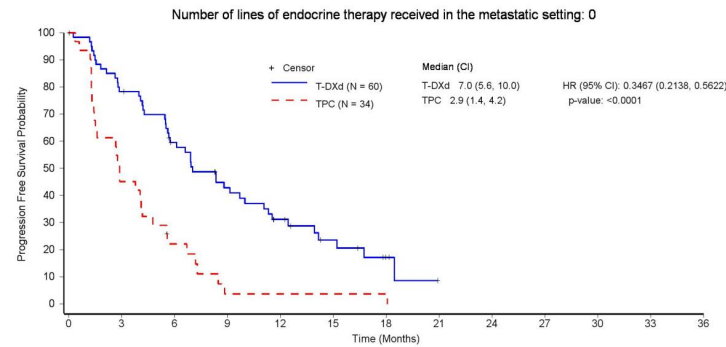
[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

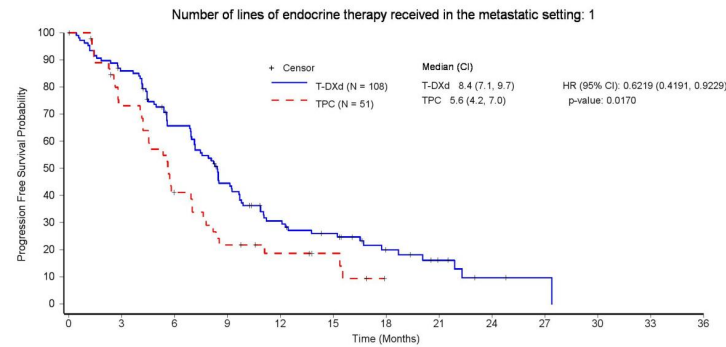
T-DXd (N = 60)	60	47	33	22	14	8	3	0	0	0	0	0	0
TPC (N = 34)	34	14	6	1	1	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:09; Program name: F1\_OS\_4\_FAS.sas; Output name: F2\_PFS\_INVE\_4\_FAS.rtf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33	36
T-DXd (N = 108)	108	91	66	43	27	21	11	6	2	1	0	0	0
TPC (N = 51)	51	32	17	9	6	4	0	0	0	0	0	0	0

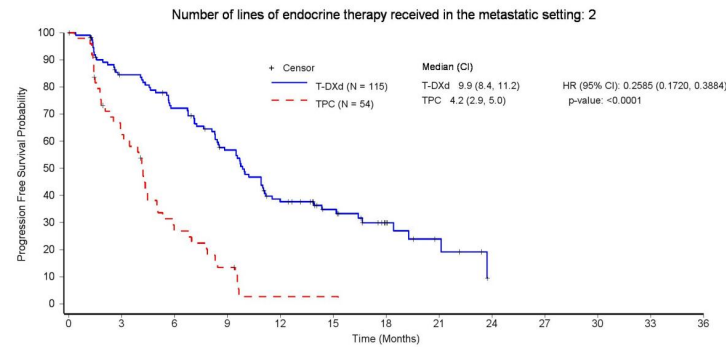
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:09; Program name: F1\_OS\_4\_FAS.sas; Output name: F2\_PFS\_INVE\_4\_FAS.rf



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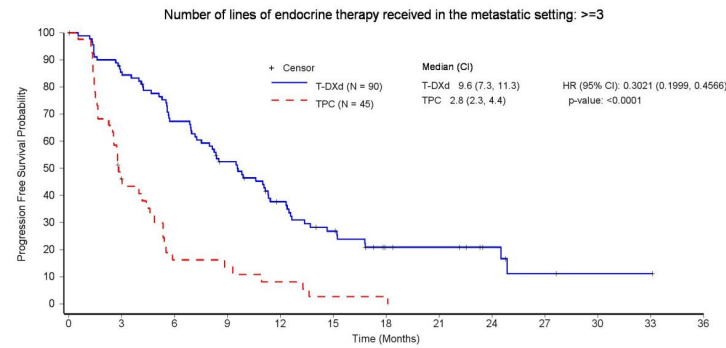
T-DXd (N = 115)	115	90	76	57	36	23	12	5	0	0	0	0	0
TPC (N = 54)	54	29	12	6	1	1	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:09; Program name: F1\_OS\_4\_FAS.sas; Output name: F2\_PFS\_INVE\_4\_FAS.rf

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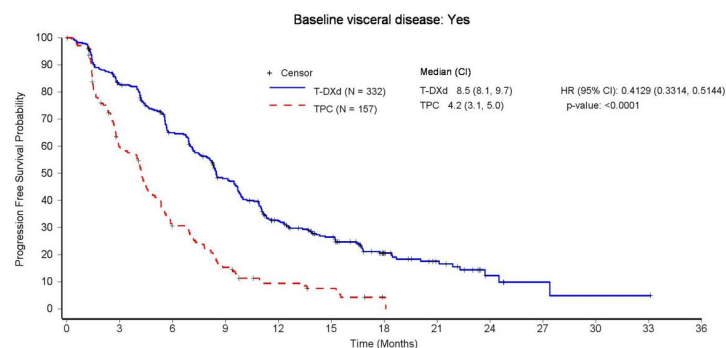
	0	3	6	9	12	15	18	21	24	27	30	33	36
T-DXd (N = 90)	90	76	59	44	28	19	10	9	5	2	1	1	0
TPC (N = 45)	45	17	6	5	3	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:09; Program name: F1\_OS\_4\_FAS.sas; Output name: F2\_PFS\_INVE\_4\_FAS.rtf

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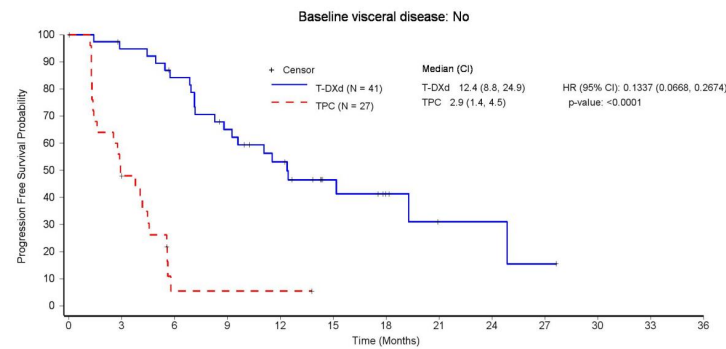
	0	3	6	9	12	15	18	21	24	27	30	33	36
T-DXd (N = 332)	332	268	203	143	88	62	31	18	5	2	1	1	0
TPC (N = 157)	157	81	40	20	10	7	2	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:09; Program name: F1\_OS\_4\_FAS.sas; Output name: F2\_PFS\_INVE\_4\_FAS.rf

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Patients still at risk:

T-DXd (N = 41)	41	36	31	23	17	9	5	2	2	1	0	0	0
TPC (N = 27)	27	11	1	1	1	0	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:09; Program name: F1\_OS\_4\_FAS.sas; Output name: F2\_PFS\_INVE\_4\_FAS.rf

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DE.T.2.8.1 - Progression-free survival 2 based on investigator's assessment - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	199 (53.4)	112 (60.9)	
Number of subjects censored, n (%)	174 (46.6)	72 (39.1)	
Median time to first event (months) [a]	15.4	10.5	
95% Confidence Interval	[13.6, 17.3]	[8.3, 11.4]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.5513
95% Confidence Interval			[0.4344, 0.6996]
p-value			<0.0001
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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DE.T.2.8.2 - Progression-free survival 2 based on investigator's assessment - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.1426
HER2 IHC 1+	214	114 (53.3)	100 (46.7)	14.9 (13.1, 17.3)	107	70 (65.4)	37 (34.6)	9.4 (7.8, 10.8)	0.4801 (0.3555, 0.6484) <0.0001	<0.0001
HER2 IHC 2+/ISH Negative	159	85 (53.5)	74 (46.5)	15.5 (12.8, 19.4)	77	42 (54.5)	35 (45.5)	11.4 (8.2, 16.9)	0.6725 (0.4636, 0.9757) 0.0367	0.0352

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.2.8.2 - Progression-free survival 2 based on investigator's assessment - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.3612
1	221	112 (50.7)	109 (49.3)	16.5 (14.4, 19.4)	100	64 (64.0)	36 (36.0)	10.5 (8.3, 11.8)	0.5077 (0.3726, 0.6917) <0.0001	<0.0001
>=2	151	87 (57.6)	64 (42.4)	13.4 (11.9, 15.5)	83	48 (57.8)	35 (42.2)	10.0 (7.3, 14.1)	0.6420 (0.4498, 0.9161) 0.0146	0.0136

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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DE.T.2.8.2 - Progression-free survival 2 based on investigator's assessment - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Prior CDK4/6											
Yes	235	135 (57.4)	100 (42.6)	14.4 (12.1, 15.5)	118	73 (61.9)	45 (38.1)	9.0 (7.8, 10.6)	0.5643 (0.4235, 0.7520) 0.0001	<0.0001	0.7694
No	98	40 (40.8)	58 (59.2)	25.1 (15.5, NE)	48	25 (52.1)	23 (47.9)	12.7 (10.7, 16.9)	0.5219 (0.3158, 0.8626) 0.0112	0.0098	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:12; Program name: T1\_OS\_2\_FAS.sas; Output name: T2\_PFS2\_BICR\_2\_FAS.rtf



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DE.T.2.8.2 - Progression-free survival 2 based on investigator's assessment - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Age										0.9877
<65	290	151 (52.1)	139 (47.9)	15.5 (13.6, 18.2)	136	77 (56.6)	59 (43.4)	10.2 (7.9, 12.5)	0.5665 (0.4297, 0.7468) 0.0001	<0.0001
>=65	83	48 (57.8)	35 (42.2)	14.8 (12.0, 17.8)	48	35 (72.9)	13 (27.1)	10.8 (8.4, 13.5)	0.5511 (0.3542, 0.8573) 0.0082	0.0075

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 13SEP2022 – 17:12; Program name: T1\_OS\_2\_FAS.sas; Output name: T2\_PFS2\_BICR\_2\_FAS.rtf

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Age										0.3293
<75	359	192 (53.5)	167 (46.5)	15.5 (13.6, 17.3)	175	106 (60.6)	69 (39.4)	10.5 (8.3, 11.4)	0.5376 (0.4231, 0.6830) <0.0001	<0.0001
>=75	14	7 (50.0)	7 (50.0)	14.9 (8.2, 19.4)	9	6 (66.7)	3 (33.3)	15.6 (4.8, 23.6)	1.2374 (0.3846, 3.9810) 0.7208	0.7204

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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DE.T.2.8.2 - Progression-free survival 2 based on investigator's assessment - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Race										0.8724
White	176	101 (57.4)	75 (42.6)	14.4 (12.9, 16.4)	91	53 (58.2)	38 (41.8)	8.3 (6.5, 10.5)	0.5502 (0.3932, 0.7700) 0.0005	0.0004
Non-White	197	98 (49.7)	99 (50.3)	16.4 (13.7, 20.1)	92	58 (63.0)	34 (37.0)	11.9 (9.4, 14.4)	0.5646 (0.4071, 0.7830) 0.0006	0.0005

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 13SEP2022 – 17:12; Program name: T1\_OS\_2\_FAS.sas; Output name: T2\_PFS2\_BICR\_2\_FAS.rtf

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Region										0.8033
Asia	147	72 (49.0)	75 (51.0)	16.4 (13.7, 25.1)	66	40 (60.6)	26 (39.4)	12.7 (9.7, 15.7)	0.5725 (0.3878, 0.8451) 0.0050	0.0044
North America	60	27 (45.0)	33 (55.0)	15.5 (11.2, 24.8)	33	16 (48.5)	17 (51.5)	11.8 (6.2, 23.6)	0.6014 (0.3187, 1.1348) 0.1165	0.1130
Europe + Israel	166	100 (60.2)	66 (39.8)	14.6 (12.7, 16.4)	85	56 (65.9)	29 (34.1)	8.3 (6.9, 10.5)	0.5087 (0.3651, 0.7086) 0.0001	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
ECOG PS										0.8946
0	200	99 (49.5)	101 (50.5)	17.3 (14.6, 20.1)	105	57 (54.3)	48 (45.7)	10.5 (8.3, 15.6)	0.5341 (0.3848, 0.7413) 0.0002	0.0001
1	173	100 (57.8)	73 (42.2)	13.6 (12.3, 15.5)	79	55 (69.6)	24 (30.4)	10.0 (7.3, 11.4)	0.5618 (0.4019, 0.7852) 0.0007	0.0006

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting										0.5088
0	60	31 (51.7)	29 (48.3)	14.9 (9.9, 19.4)	34	24 (70.6)	10 (29.4)	7.5 (5.1, 11.4)	0.4878 (0.2856, 0.8330)	0.0073
1	108	54 (50.0)	54 (50.0)	15.4 (12.7, 20.1)	51	29 (56.9)	22 (43.1)	11.4 (9.0, 15.6)	0.6881 (0.4376, 1.0822)	0.1050
2	115	58 (50.4)	57 (49.6)	16.4 (13.1, 24.5)	54	33 (61.1)	21 (38.9)	9.4 (7.2, 13.5)	0.4409 (0.2847, 0.6828)	0.0002
>=3	90	56 (62.2)	34 (37.8)	14.4 (12.3, 17.5)	45	26 (57.8)	19 (42.2)	10.8 (6.5, 16.9)	0.6253 (0.3908, 1.0006)	0.0479

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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DE.T.2.8.2 - Progression-free survival 2 based on investigator's assessment - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.4789
PD	174	93 (53.4)	81 (46.6)	14.4 (12.8, 16.4)	85	52 (61.2)	33 (38.8)	8.9 (6.5, 11.4)	0.5577 (0.3964, 0.7846)	0.0007
PR	48	29 (60.4)	19 (39.6)	17.0 (12.3, 23.7)	22	16 (72.7)	6 (27.3)	9.0 (4.8, 16.2)	0.4052 (0.2160, 0.7600)	0.0036
SD	82	47 (57.3)	35 (42.7)	15.1 (12.0, 19.7)	55	33 (60.0)	22 (40.0)	11.4 (8.8, 16.9)	0.6814 (0.4344, 1.0690)	0.0923

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.4682
Yes	37	24 (64.9)	13 (35.1)	13.6 (9.0, 17.3)	15	8 (53.3)	7 (46.7)	7.3 (2.9, NE)	0.7163 (0.3164, 1.6219)	0.4200
No	336	175 (52.1)	161 (47.9)	15.5 (13.8, 17.8)	169	104 (61.5)	65 (38.5)	10.5 (8.4, 11.4)	0.5364 (0.4201, 0.6850)	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.3540
Yes	24	14 (58.3)	10 (41.7)	13.7 (9.0, 24.5)	8	4 (50.0)	4 (50.0)	7.5 (0.6, NE)	0.9180 (0.2983, 2.8255)	0.8814
No	349	185 (53.0)	164 (47.0)	15.5 (13.8, 17.5)	176	108 (61.4)	68 (38.6)	10.5 (8.4, 11.4)	0.5388 (0.4242, 0.6845)	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Renal function at baseline											0.0285
Normal Function	202	102 (50.5)	100 (49.5)	15.6 (13.3, 18.5)	87	56 (64.4)	31 (35.6)	8.3 (7.2, 10.5)	0.4267 (0.3069, 0.5934) <0.0001	<0.0001	
Mild Impairment	123	70 (56.9)	53 (43.1)	14.6 (12.4, 18.2)	69	39 (56.5)	30 (43.5)	10.5 (7.9, 14.1)	0.5890 (0.3952, 0.8779) 0.0093	0.0086	
Moderate Impairment	41	23 (56.1)	18 (43.9)	14.9 (10.9, 18.2)	23	14 (60.9)	9 (39.1)	15.6 (11.4, 23.6)	1.1924 (0.6122, 2.3227) 0.6049	0.5977	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hepatic function at baseline											0.0804
Normal Function	170	87 (51.2)	83 (48.8)	16.4 (14.9, 21.2)	98	54 (55.1)	44 (44.9)	11.9 (10.8, 16.6)	0.6094 (0.4329, 0.8578) 0.0045	0.0041	
Mild Impairment	195	106 (54.4)	89 (45.6)	13.6 (11.5, 16.5)	84	57 (67.9)	27 (32.1)	7.8 (5.8, 8.4)	0.4266 (0.3076, 0.5916) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline visceral disease										0.6018
Yes	332	181 (54.5)	151 (45.5)	14.8 (13.1, 16.5)	157	96 (61.1)	61 (38.9)	9.7 (8.0, 10.8)	0.5635 (0.4393, 0.7229) <0.0001	<0.0001
No	41	18 (43.9)	23 (56.1)	17.3 (14.9, 28.1)	27	16 (59.3)	11 (40.7)	12.7 (7.2, 17.2)	0.4082 (0.2029, 0.8214) 0.0120	0.0093

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (IXRS)										0.8473
Positive	331	172 (52.0)	159 (48.0)	15.5 (13.8, 17.5)	163	96 (58.9)	67 (41.1)	10.5 (8.4, 11.9)	0.5572 (0.4333, 0.7164) <0.0001	<0.0001
Negative	42	27 (64.3)	15 (35.7)	12.9 (9.0, 18.2)	21	16 (76.2)	5 (23.8)	8.9 (5.1, 12.7)	0.5406 (0.2886, 1.0124) 0.0547	0.0517

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (derived)										0.8422
Positive	333	174 (52.3)	159 (47.7)	15.5 (14.4, 17.5)	166	98 (59.0)	68 (41.0)	10.5 (8.4, 11.8)	0.5566 (0.4338, 0.7142) <0.0001	<0.0001
Negative	40	25 (62.5)	15 (37.5)	12.9 (9.6, 18.2)	18	14 (77.8)	4 (22.2)	8.9 (5.0, 14.1)	0.5375 (0.2773, 1.0417) 0.0659	0.0618

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

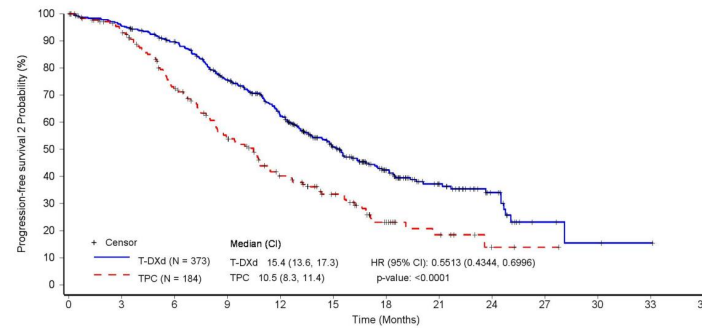
[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:12; Program name: T1\_OS\_2\_FAS.sas; Output name: T2\_PFS2\_BICR\_2\_FAS.rtf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33	36
T-DXd (N = 373)	373	354	321	261	196	128	78	43	19	4	2	1	0
TPC (N = 184)	184	184	156	115	81	52	34	16	8	2	1	0	0

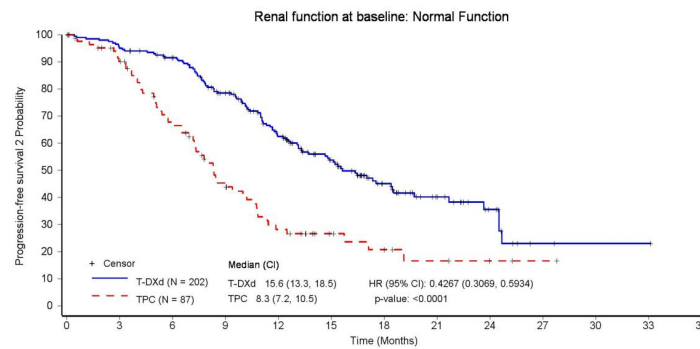
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:10; Program name: F1\_OS\_3\_FAS.sas; Output name: F2\_PFS2\_BICR\_3\_FAS.rtf

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DE.F.2.8.4 - Progression-free survival 2 based on investigator's assessment - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33	36
T-DXd (N = 202)	202	192	178	146	106	71	41	23	11	2	1	1	0
TPC (N = 87)	87	72	50	31	18	10	7	4	2	1	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

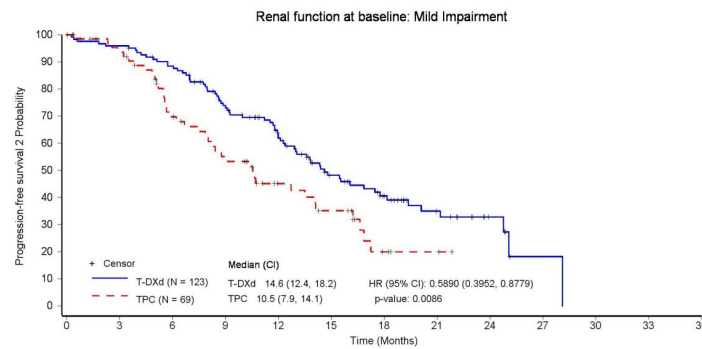
Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:10; Program name: F1\_OS\_4\_FAS.sas; Output name: F2\_PFS2\_BICR\_4\_FAS.rf



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DE.F.2.8.4 - Progression-free survival 2 based on investigator's assessment - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33	36
T-DXd (N = 123)	123	117	106	85	64	41	28	16	6	1	0	0	0
TPC (N = 69)	69	58	40	29	18	13	4	2	0	0	0	0	0

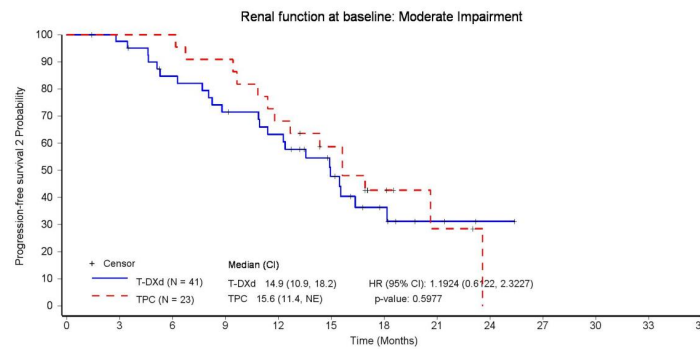
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:10; Program name: F1\_OS\_4\_FAS.sas; Output name: F2\_PFS2\_BICR\_4\_FAS.rf

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DE.F.2.8.4 - Progression-free survival 2 based on investigator's assessment - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33	36
T-DXd (N = 41)	41	40	32	27	23	14	7	3	1	0	0	0	0
TPC (N = 23)	23	22	22	20	15	11	5	2	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:10; Program name: F1\_OS\_4\_FAS.sas; Output name: F2\_PFS2\_BICR\_4\_FAS.rf

**Anhang 4-G 2.2: Tumoransprechen**

**Anhang 4-G 2.2.1: Objektive Ansprechrates**

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DE.T.2.3.1 - Confirmed objective response rate based on BICR - Analysis of dichotomous endpoints - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

	T-DXd (N=373)	TPC (N=184)	T-DXd vs TPC
Number of subjects with events, n (%)	195 (52.3)	30 (16.3)	
95% CI [a]	(47.1, 57.4)	(11.3, 22.5)	
Odds ratio (95% CI) [b]			5.62 (3.62, 8.74)
Relative risk (95% CI) [b]			3.21 (2.28, 4.51)
Absolute risk reduction (95% CI) [b]			35.97 (28.21, 43.74)
p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value based on the Cochran-Mantel-Haenszel test adjusted for randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 13SEP2022 – 17:11; Program name: T2\_ORR\_BICR\_1\_FAS.sas; Output name: T2\_ORR\_BICR\_1\_FAS.rtf

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction	
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)		p-value [c]
HER2 status									0.5370
HER2 IHC 1+	214	105 (49.1) (42.2, 56.0)	107	18 (16.8) (10.3, 25.3)	4.76 (2.69, 8.45)	2.92 (1.87, 4.54)	32.24 (21.79, 42.70)	<0.0001	
HER2 IHC 2+/ISH Negative	159	90 (56.6) (48.5, 64.4)	77	12 (15.6) (8.3, 25.6)	7.07 (3.54, 14.10)	3.63 (2.12, 6.22)	41.02 (28.88, 53.16)	<0.0001	
Number of prior lines of chemotherapy in a metastatic setting									0.2604
1	221	113 (51.1) (44.3, 57.9)	100	19 (19.0) (11.8, 28.1)	4.46 (2.54, 7.85)	2.69 (1.76, 4.12)	32.13 (21.28, 42.98)	<0.0001	
>=2	151	81 (53.6) (45.4, 61.8)	83	11 (13.3) (6.8, 22.5)	7.57 (3.72, 15.41)	4.05 (2.29, 7.16)	40.39 (28.66, 52.12)	<0.0001	

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction p-value [d]
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	
Prior CDK4/6								0.1455
Yes	235	118 (50.2) (43.6, 56.8)	118	15 (12.7) (7.3, 20.1)	6.93 (3.80, 12.61)	3.95 (2.42, 6.45)	37.50 (28.09, 46.91)	<0.0001
No	98	57 (58.2) (47.8, 68.1)	48	12 (25.0) (13.6, 39.6)	4.17 (1.94, 8.98)	2.33 (1.39, 3.91)	33.16 (15.94, 50.38)	0.0002
Age								0.1936
<65	290	156 (53.8) (47.9, 59.6)	136	20 (14.7) (9.2, 21.8)	6.75 (3.98, 11.45)	3.66 (2.41, 5.56)	39.09 (30.28, 47.89)	<0.0001
>=65	83	39 (47.0) (35.9, 58.3)	48	10 (20.8) (10.5, 35.0)	3.37 (1.48, 7.64)	2.26 (1.24, 4.10)	26.15 (8.79, 43.52)	0.0030

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

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DE.T.2.3.2 - Confirmed objective response rate based on BICR - Analysis of dichotomous endpoints - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction p-value [d]
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	
Age								0.1536
<75	359	188 (52.4) (47.1, 57.6)	175	27 (15.4) (10.4, 21.6)	6.03 (3.81, 9.54)	3.39 (2.37, 4.87)	36.94 (29.08, 44.80)	<0.0001
>=75	14	7 (50.0) (23.0, 77.0)	9	3 (33.3) (7.5, 70.1)	2.00 (0.35, 11.36)	1.50 (0.52, 4.34)	16.67 (-32.89, 66.22)	0.4415
Race								0.7667
White	176	94 (53.4) (45.8, 60.9)	91	16 (17.6) (10.4, 27.0)	5.37 (2.90, 9.95)	3.04 (1.91, 4.84)	35.83 (24.25, 47.41)	<0.0001
Non-White	197	101 (51.3) (44.1, 58.4)	92	14 (15.2) (8.6, 24.2)	5.86 (3.11, 11.05)	3.37 (2.04, 5.56)	36.05 (25.13, 46.98)	<0.0001

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction p-value [d]
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	
Region								0.3838
Asia	147	79 (53.7) (45.3, 62.0)	66	9 (13.6) (6.4, 24.3)	7.36 (3.39, 15.96)	3.94 (2.11, 7.37)	40.11 (27.45, 52.76)	<0.0001
North America	60	26 (43.3) (30.6, 56.8)	33	7 (21.2) (9.0, 38.9)	2.84 (1.07, 7.56)	2.04 (1.00, 4.19)	22.12 (1.02, 43.23)	0.0339
Europe + Israel	166	90 (54.2) (46.3, 62.0)	85	14 (16.5) (9.3, 26.1)	6.01 (3.14, 11.50)	3.29 (2.00, 5.42)	37.75 (25.92, 49.57)	<0.0001
ECOG PS								0.7582
0	200	109 (54.5) (47.3, 61.5)	105	17 (16.2) (9.7, 24.7)	6.20 (3.44, 11.18)	3.37 (2.14, 5.30)	38.31 (27.72, 48.90)	<0.0001
1	173	86 (49.7) (42.0, 57.4)	79	13 (16.5) (9.1, 26.5)	5.02 (2.58, 9.76)	3.02 (1.80, 5.08)	33.26 (21.27, 45.24)	<0.0001

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.



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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction	
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting									0.5601
0	60	29 (48.3) (35.2, 61.6)	34	6 (17.6) (6.8, 34.5)	4.37 (1.58, 12.07)	2.74 (1.27, 5.93)	30.69 (10.38, 50.99)	0.0033	
1	108	61 (56.5) (46.6, 66.0)	51	10 (19.6) (9.8, 33.1)	5.32 (2.42, 11.71)	2.88 (1.61, 5.14)	36.87 (21.07, 52.68)	<0.0001	
2	115	58 (50.4) (41.0, 59.9)	54	10 (18.5) (9.3, 31.4)	4.48 (2.06, 9.75)	2.72 (1.51, 4.90)	31.92 (16.74, 47.09)	<0.0001	
>=3	90	47 (52.2) (41.4, 62.9)	45	4 (8.9) (2.5, 21.2)	11.20 (3.70, 33.89)	5.88 (2.26, 15.28)	43.33 (28.41, 58.25)	<0.0001	

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC				Interaction p-value [d]
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	p-value [c]	
Best Response to last prior cancer systemic therapy									0.7148
PD	174	88 (50.6) (42.9, 58.2)	85	14 (16.5) (9.3, 26.1)	5.19 (2.72, 9.90)	3.07 (1.86, 5.07)	34.10 (22.40, 45.81)	<0.0001	
PR	48	31 (64.6) (49.5, 77.8)	22	3 (13.6) (2.9, 34.9)	11.55 (2.98, 44.72)	4.74 (1.62, 13.84)	50.95 (27.92, 73.98)	<0.0001	
SD	82	38 (46.3) (35.3, 57.7)	55	9 (16.4) (7.8, 28.8)	4.41 (1.91, 10.18)	2.83 (1.49, 5.38)	29.98 (13.90, 46.06)	0.0003	
Reported history of CNS metastases									0.3849
Yes	37	18 (48.6) (31.9, 65.6)	15	1 (6.7) (0.2, 31.9)	13.26 (1.58, 111.46)	7.30 (1.07, 49.89)	41.98 (16.83, 67.13)	0.0048	
No	336	177 (52.7) (47.2, 58.1)	169	29 (17.2) (11.8, 23.7)	5.37 (3.41, 8.46)	3.07 (2.17, 4.34)	35.52 (27.28, 43.76)	<0.0001	

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction p-value [d]
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	
Baseline CNS metastases								0.4561
Yes	24	12 (50.0) (29.1, 70.9)	8	2 (25.0) (3.2, 65.1)	3.00 (0.50, 17.95)	2.00 (0.56, 7.09)	25.00 (-19.40, 69.40)	0.2244
No	349	183 (52.4) (47.1, 57.8)	176	28 (15.9) (10.8, 22.2)	5.83 (3.70, 9.19)	3.30 (2.31, 4.70)	36.53 (28.57, 44.48)	<0.0001
Renal function at baseline								0.0480
Normal Function	202	104 (51.5) (44.4, 58.6)	87	11 (12.6) (6.5, 21.5)	7.33 (3.68, 14.62)	4.07 (2.31, 7.19)	38.84 (28.21, 49.48)	<0.0001
Mild Impairment	123	67 (54.5) (45.2, 63.5)	69	11 (15.9) (8.2, 26.7)	6.31 (3.02, 13.17)	3.42 (1.94, 6.01)	38.53 (25.07, 51.99)	<0.0001
Moderate Impairment	41	21 (51.2) (35.1, 67.1)	23	8 (34.8) (16.4, 57.3)	1.97 (0.69, 5.65)	1.47 (0.78, 2.78)	16.44 (-11.71, 44.59)	0.2086

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction p-value [d]	
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)		p-value [c]
Hepatic function at baseline									
Normal Function	170	96 (56.5) (48.7, 64.0)	98	17 (17.3) (10.4, 26.3)	6.18 (3.38, 11.31)	3.26 (2.07, 5.11)	39.12 (27.75, 50.50)	<0.0001	0.9711
Mild Impairment	195	97 (49.7) (42.5, 57.0)	84	13 (15.5) (8.5, 25.0)	5.41 (2.81, 10.40)	3.21 (1.91, 5.40)	34.27 (22.97, 45.56)	<0.0001	
Baseline visceral disease									
Yes	332	173 (52.1) (46.6, 57.6)	157	29 (18.5) (12.7, 25.4)	4.80 (3.04, 7.58)	2.82 (2.00, 3.98)	33.64 (25.06, 42.21)	<0.0001	0.1043
No	41	22 (53.7) (37.4, 69.3)	27	1 (3.7) (0.1, 19.0)	30.11 (3.73, 243.28)	14.49 (2.07, 101.25)	49.95 (30.04, 69.87)	<0.0001	

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

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DE.T.2.3.2 - Confirmed objective response rate based on BICR - Analysis of dichotomous endpoints - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction	
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)		p-value [c]
Hormon receptor status (IXRS)									0.9412
Positive	331	175 (52.9) (47.3, 58.4)	163	27 (16.6) (11.2, 23.2)	5.65 (3.55, 9.00)	3.19 (2.23, 4.57)	36.31 (28.01, 44.61)	<0.0001	
Negative	42	20 (47.6) (32.0, 63.6)	21	3 (14.3) (3.0, 36.3)	5.45 (1.39, 21.34)	3.33 (1.12, 9.96)	33.33 (8.50, 58.17)	0.0102	
Hormon receptor status (derived)									0.8982
Positive	333	175 (52.6) (47.0, 58.0)	166	27 (16.3) (11.0, 22.8)	5.70 (3.58, 9.08)	3.23 (2.25, 4.63)	36.29 (28.07, 44.50)	<0.0001	
Negative	40	20 (50.0) (33.8, 66.2)	18	3 (16.7) (3.6, 41.4)	5.00 (1.25, 19.99)	3.00 (1.02, 8.82)	33.33 (6.14, 60.52)	0.0173	

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

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DE.T.2.3.3 - Confirmed objective response rate based on investigator's assessment - Analysis of dichotomous endpoints - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

	T-DXd (N=373)	TPC (N=184)	T-DXd vs TPC
Number of subjects with events, n (%)	193 (51.7)	31 (16.8)	
95% CI [a]	(46.5, 56.9)	(11.7, 23.1)	
Odds ratio (95% CI) [b]			5.29 (3.42, 8.19)
Relative risk (95% CI) [b]			3.07 (2.20, 4.30)
Absolute risk reduction (95% CI) [b]			34.89 (27.08, 42.71)
p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value based on the Cochran-Mantel-Haenszel test adjusted for randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 13SEP2022 – 17:11; Program name: T2\_ORR\_BICR\_1\_FAS.sas; Output name: T2\_ORR\_INVE\_3\_FAS.rtf

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction	
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	p-value [c]	p-value [d]
HER2 status									0.4753
HER2 IHC 1+	214	105 (49.1) (42.2, 56.0)	107	19 (17.8) (11.0, 26.3)	4.46 (2.54, 7.84)	2.76 (1.80, 4.25)	31.31 (20.74, 41.87)	<0.0001	
HER2 IHC 2+/ISH Negative	159	88 (55.3) (47.3, 63.2)	77	12 (15.6) (8.3, 25.6)	6.71 (3.37, 13.39)	3.55 (2.07, 6.08)	39.76 (27.60, 51.92)	<0.0001	
Number of prior lines of chemotherapy in a metastatic setting									0.1041
1	221	106 (48.0) (41.2, 54.8)	100	20 (20.0) (12.7, 29.2)	3.69 (2.11, 6.43)	2.40 (1.58, 3.63)	27.96 (17.00, 38.93)	<0.0001	
>=2	151	86 (57.0) (48.7, 65.0)	83	11 (13.3) (6.8, 22.5)	8.66 (4.25, 17.64)	4.30 (2.44, 7.58)	43.70 (32.02, 55.38)	<0.0001	

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

NE - Not Evaluable

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC				Interaction
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	p-value [c]	p-value [d]
Prior CDK4/6									0.1739
Yes	235	118 (50.2) (43.6, 56.8)	118	18 (15.3) (9.3, 23.0)	5.60 (3.19, 9.84)	3.29 (2.11, 5.13)	34.96 (25.21, 44.70)	<0.0001	
No	98	50 (51.0) (40.7, 61.3)	48	12 (25.0) (13.6, 39.6)	3.13 (1.46, 6.71)	2.04 (1.20, 3.46)	26.02 (8.72, 43.32)	0.0029	
Age									0.5034
<65	290	153 (52.8) (46.8, 58.6)	136	25 (18.4) (12.3, 25.9)	4.96 (3.03, 8.10)	2.87 (1.98, 4.16)	34.38 (25.15, 43.60)	<0.0001	
>=65	83	40 (48.2) (37.1, 59.4)	48	6 (12.5) (4.7, 25.2)	6.51 (2.50, 16.97)	3.86 (1.77, 8.42)	35.69 (19.80, 51.59)	<0.0001	

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

NE - Not Evaluable



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DE.T.2.3.4 - Confirmed objective response rate based on investigator's assessment - Analysis of dichotomous endpoints - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction	
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	p-value [c]	p-value [d]
Age									0.2562
<75	359	185 (51.5) (46.2, 56.8)	175	28 (16.0) (10.9, 22.3)	5.58 (3.54, 8.79)	3.22 (2.26, 4.59)	35.53 (27.61, 43.46)	<0.0001	
>=75	14	8 (57.1) (28.9, 82.3)	9	3 (33.3) (7.5, 70.1)	2.67 (0.47, 15.25)	1.71 (0.61, 4.80)	23.81 (-25.57, 73.19)	0.2752	
Race									0.9270
White	176	90 (51.1) (43.5, 58.7)	91	15 (16.5) (9.5, 25.7)	5.30 (2.83, 9.93)	3.10 (1.91, 5.04)	34.65 (23.21, 46.10)	<0.0001	
Non-White	197	103 (52.3) (45.1, 59.4)	92	16 (17.4) (10.3, 26.7)	5.20 (2.84, 9.55)	3.01 (1.89, 4.79)	34.89 (23.67, 46.11)	<0.0001	

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

NE - Not Evaluable

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction	
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	p-value [c]	p-value [d]
Region									0.5540
Asia	147	74 (50.3) (42.0, 58.7)	66	11 (16.7) (8.6, 27.9)	5.07 (2.46, 10.45)	3.02 (1.72, 5.30)	33.67 (20.49, 46.86)	<0.0001	
North America	60	28 (46.7) (33.7, 60.0)	33	7 (21.2) (9.0, 38.9)	3.25 (1.22, 8.63)	2.20 (1.08, 4.48)	25.45 (4.29, 46.62)	0.0159	
Europe + Israel	166	91 (54.8) (46.9, 62.5)	85	13 (15.3) (8.4, 24.7)	6.72 (3.46, 13.07)	3.58 (2.13, 6.02)	39.53 (27.87, 51.18)	<0.0001	
ECOG PS									0.7278
0	200	106 (53.0) (45.8, 60.1)	105	19 (18.1) (11.3, 26.8)	5.10 (2.89, 9.02)	2.93 (1.91, 4.49)	34.90 (24.08, 45.73)	<0.0001	
1	173	87 (50.3) (42.6, 58.0)	79	12 (15.2) (8.1, 25.0)	5.65 (2.85, 11.18)	3.31 (1.93, 5.69)	35.10 (23.31, 46.89)	<0.0001	

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

NE - Not Evaluable

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction	
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting									0.3200
0	60	32 (53.3) (40.0, 66.3)	34	4 (11.8) (3.3, 27.5)	8.57 (2.69, 27.34)	4.53 (1.75, 11.73)	41.57 (22.63, 60.50)	<0.0001	
1	108	58 (53.7) (43.8, 63.3)	51	12 (23.5) (12.8, 37.5)	3.77 (1.78, 7.98)	2.28 (1.35, 3.86)	30.17 (13.77, 46.58)	0.0004	
2	115	60 (52.2) (42.7, 61.6)	54	6 (11.1) (4.2, 22.6)	8.73 (3.46, 21.99)	4.70 (2.16, 10.19)	41.06 (27.31, 54.82)	<0.0001	
>=3	90	43 (47.8) (37.1, 58.6)	45	9 (20.0) (9.6, 34.6)	3.66 (1.58, 8.47)	2.39 (1.28, 4.45)	27.78 (10.52, 45.04)	0.0018	

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

NE - Not Evaluable

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC				Interaction
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy									0.1452
PD	174	96 (55.2) (47.5, 62.7)	85	11 (12.9) (6.6, 22.0)	8.28 (4.11, 16.68)	4.26 (2.42, 7.52)	42.23 (31.08, 53.38)	<0.0001	
PR	48	31 (64.6) (49.5, 77.8)	22	3 (13.6) (2.9, 34.9)	11.55 (2.98, 44.72)	4.74 (1.62, 13.84)	50.95 (27.92, 73.98)	<0.0001	
SD	82	33 (40.2) (29.6, 51.7)	55	11 (20.0) (10.4, 33.0)	2.69 (1.22, 5.96)	2.01 (1.11, 3.63)	20.24 (3.74, 36.74)	0.0132	
Reported history of CNS metastases									0.3007
Yes	37	20 (54.1) (36.9, 70.5)	15	1 (6.7) (0.2, 31.9)	16.47 (1.96, 138.50)	8.11 (1.19, 55.12)	47.39 (22.28, 72.50)	0.0018	
No	336	173 (51.5) (46.0, 56.9)	169	30 (17.8) (12.3, 24.4)	4.92 (3.14, 7.70)	2.90 (2.06, 4.08)	33.74 (25.43, 42.04)	<0.0001	

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

NE - Not Evaluable

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction	
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	p-value [c]	p-value [d]
Baseline CNS metastases									0.6626
Yes	24	14 (58.3) (36.6, 77.9)	8	2 (25.0) (3.2, 65.1)	4.20 (0.70, 25.26)	2.33 (0.67, 8.12)	33.33 (-10.91, 77.57)	0.1080	
No	349	179 (51.3) (45.9, 56.6)	176	29 (16.5) (11.3, 22.8)	5.34 (3.40, 8.37)	3.11 (2.20, 4.41)	34.81 (26.80, 42.82)	<0.0001	
Renal function at baseline									0.0532
Normal Function	202	105 (52.0) (44.9, 59.0)	87	15 (17.2) (10.0, 26.8)	5.20 (2.79, 9.67)	3.01 (1.87, 4.87)	34.74 (23.41, 46.07)	<0.0001	
Mild Impairment	123	68 (55.3) (46.1, 64.3)	69	8 (11.6) (5.1, 21.6)	9.43 (4.16, 21.37)	4.77 (2.44, 9.32)	43.69 (30.97, 56.41)	<0.0001	
Moderate Impairment	41	18 (43.9) (28.5, 60.3)	23	7 (30.4) (13.2, 52.9)	1.79 (0.61, 5.27)	1.44 (0.71, 2.93)	13.47 (-14.10, 41.03)	0.2931	

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

NE - Not Evaluable

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction	
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	p-value [c]	p-value [d]
Hepatic function at baseline									0.5910
Normal Function	170	95 (55.9) (48.1, 63.5)	98	19 (19.4) (12.1, 28.6)	5.27 (2.93, 9.46)	2.88 (1.88, 4.41)	36.49 (24.87, 48.11)	<0.0001	
Mild Impairment	195	97 (49.7) (42.5, 57.0)	84	12 (14.3) (7.6, 23.6)	5.94 (3.03, 11.64)	3.48 (2.02, 5.99)	35.46 (24.35, 46.57)	<0.0001	
Baseline visceral disease									0.0852
Yes	332	171 (51.5) (46.0, 57.0)	157	31 (19.7) (13.8, 26.8)	4.32 (2.76, 6.76)	2.61 (1.87, 3.64)	31.76 (23.07, 40.46)	<0.0001	
No	41	22 (53.7) (37.4, 69.3)	157	126 (80.3) (73.2, 86.2)	NE (NE, NE)	NE (NE, NE)	53.66 (35.32, 71.99)	<0.0001	

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

NE - Not Evaluable

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DE.T.2.3.4 - Confirmed objective response rate based on investigator's assessment - Analysis of dichotomous endpoints - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC				Interaction
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	p-value [c]	p-value [d]
Hormon receptor status (IXRS)									0.1305
Positive	331	168 (50.8) (45.2, 56.3)	163	30 (18.4) (12.8, 25.2)	4.57 (2.91, 7.17)	2.76 (1.96, 3.88)	32.35 (23.87, 40.83)	<0.0001	
Negative	42	25 (59.5) (43.3, 74.4)	21	1 (4.8) (0.1, 23.8)	29.41 (3.60, 240.36)	12.50 (1.82, 86.03)	54.76 (33.77, 75.75)	<0.0001	
Hormon receptor status (derived)									0.1478
Positive	333	167 (50.2) (44.6, 55.6)	166	30 (18.1) (12.5, 24.8)	4.56 (2.91, 7.15)	2.77 (1.97, 3.90)	32.08 (23.68, 40.47)	<0.0001	
Negative	40	26 (65.0) (48.3, 79.4)	18	1 (5.6) (0.1, 27.3)	31.57 (3.79, 262.73)	11.70 (1.72, 79.67)	59.44 (37.24, 81.65)	<0.0001	

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

NE - Not Evaluable

**Anhang 4-G 2.2.2: Summe der längsten Durchmesser**



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DE.T.2.9.1 - Best percent change in the sum of the diameter of measurable tumors based on BICR - Analysis of continuous endpoints - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

	T-DXd (N=373)	TPC (N=184)
<b>Results (Unit)</b>		
n	348	156
Mean (SD)	41.5(37.20)	63.1(47.97)
Median	32.5	52.0
Q1, Q3	14.0, 56.0	31.0, 86.5
Min, Max	(0, 216)	(0, 315)
<b>Change from Baseline (Unit)</b>		
n	348	156
Mean (SD)	-24.6(25.75)	-8.3(25.14)
Median	-21.0	-6.0
Q1, Q3	-38.0, -6.5	-16.0, 3.5
Min, Max	(-126, 29)	(-120, 95)

N: number of subjects in analysis set; n: number of observed values;  
 [a] LSMeans obtained from a linear model adjusting for treatment and baseline value.

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DE.T.2.9.1 - Best percent change in the sum of the diameter of measurable tumors based on BICR - Analysis of continuous endpoints - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

	T-DXd (N=373)	TPC (N=184)
Percent Change from Baseline (%)		
n	348	156
Mean (SD)	-40.9(34.15)	-13.3(30.18)
Median	-42.0	-10.5
Q1, Q3	-66.0, -14.0	-31.0, 5.0
Min, Max	(-100, 46)	(-100, 52)
LSMean (95% CI) [a]	-40.73 (-44.16, -37.30)	-13.77 (-18.90, -8.65)
Difference of LSMeans (95% CI)	-26.96 (-33.13, -20.79)	
p-value	<0.0001	
Hegdes' g (95% CI)	-0.82 (-1.02, -0.63)	

N: number of subjects in analysis set; n: number of observed values;  
 [a] LSMean obtained from a linear model adjusting for treatment and baseline value.

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DE.T.2.9.2 - Best percent change in the sum of the diameter of measurable tumors based on BICR - Analysis of continuous endpoints - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd			TPC			Difference of LSMeans (95% CI)	P-value	Hedges' g (95% CI)	Interaction P-value [b]
	Nsub	Mean (SD)	LSMean (95% CI) [a]	Nsub	Mean (SD)	LSMean (95% CI) [a]				
HER2 status										0.2880
HER2 IHC 1+	197	-39.3(35.42)	-39.10 (-43.81, -34.38)	90	-14.7(31.15)	-15.14 (-22.12, -8.17)	-23.95 (-32.38, -15.53)	<0.0001	-0.71 (-0.96, -0.45)	
HER2 IHC 2+/ISH Negative	151	-43.0(32.42)	-42.86 (-47.83, -37.89)	66	-11.5(28.95)	-11.93 (-19.46, -4.40)	-30.93 (-39.96, -21.90)	<0.0001	-0.99 (-1.29, -0.68)	
Number of prior lines of chemotherapy in a metastatic setting										0.1936
1	205	-40.2(35.26)	-40.19 (-44.82, -35.57)	82	-17.2(30.95)	-17.07 (-24.38, -9.76)	-23.12 (-31.77, -14.47)	<0.0001	-0.68 (-0.94, -0.42)	
>=2	142	-41.9(32.67)	-41.44 (-46.58, -36.30)	74	-9.1(28.93)	-10.04 (-17.18, -2.89)	-31.40 (-40.24, -22.56)	<0.0001	-1.00 (-1.30, -0.70)	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category;

[a] LSMean obtained from a linear model adjusting for treatment and baseline value.

[b] Two-sided interaction p-value is for the interaction term from a linear model adjusting for treatment, baseline value, subgroup and treatment-by-subgroup interaction.

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DE.T.2.9.2 - Best percent change in the sum of the diameter of measurable tumors based on BICR - Analysis of continuous endpoints - subgroup analysis - Destiny Breast 04 - DCO  
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Subgroup	T-DXd			TPC			Difference of LSMeans (95% CI)	P-value	Hedges' g (95% CI)	Interaction P-value [b]
	Nsub	Mean (SD)	LSMean (95% CI) [a]	Nsub	Mean (SD)	LSMean (95% CI) [a]				
Prior CDK4/6										0.6199
Yes	221	-40.1(36.12)	-39.99 (-44.45, -35.54)	99	-14.3(29.08)	-14.51 (-21.16, -7.85)	-25.49 (-33.50, -17.48)	<0.0001	-0.75 (-1.00, -0.51)	
No	92	-44.0(29.87)	-43.70 (-49.87, -37.53)	40	-13.5(30.88)	-14.17 (-23.56, -4.77)	-29.53 (-40.82, -18.24)	<0.0001	-0.97 (-1.36, -0.58)	
Age										0.7547
<65	270	-41.3(33.81)	-41.24 (-45.14, -37.35)	115	-13.6(31.18)	-13.81 (-19.78, -7.84)	-27.44 (-34.56, -20.31)	<0.0001	-0.84 (-1.06, -0.61)	
>=65	78	-39.5(35.49)	-38.95 (-46.28, -31.61)	41	-12.6(27.54)	-13.71 (-23.89, -3.54)	-25.23 (-37.87, -12.59)	<0.0001	-0.76 (-1.15, -0.37)	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category;

[a] LSMean obtained from a linear model adjusting for treatment and baseline value.

[b] Two-sided interaction p-value is for the interaction term from a linear model adjusting for treatment, baseline value, subgroup and treatment-by-subgroup interaction.

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Subgroup	T-DXd			TPC			Difference of LSMeans (95% CI)	P-value	Hedges' g (95% CI)	Interaction P-value [b]
	Nsub	Mean (SD)	LSMean (95% CI) [a]	Nsub	Mean (SD)	LSMean (95% CI) [a]				
Age										0.4724
<75	335	-41.1(34.31)	-40.89 (-44.40, -37.37)	147	-13.0(30.61)	-13.43 (-18.74, -8.12)	-27.46 (-33.83, -21.09)	<0.0001	-0.83 (-1.04, -0.63)	
>=75	13	-37.8(30.88)	-37.97 (-53.88, -22.06)	9	-18.0(22.83)	-17.71 (-37.00, 1.58)	-20.26 (-45.86, 5.34)	0.1209	-0.66 (-1.54, 0.21)	
Race										0.0756
White	165	-40.0(33.32)	-40.09 (-45.00, -35.17)	76	-19.3(30.08)	-19.18 (-26.43, -11.94)	-20.90 (-29.66, -12.15)	<0.0001	-0.65 (-0.92, -0.37)	
Non-White	183	-41.7(34.95)	-41.23 (-46.00, -36.46)	79	-8.2(29.21)	-9.36 (-16.64, -2.08)	-31.87 (-40.60, -23.13)	<0.0001	-0.96 (-1.24, -0.69)	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category;

[a] LSMean obtained from a linear model adjusting for treatment and baseline value.

[b] Two-sided interaction p-value is for the interaction term from a linear model adjusting for treatment, baseline value, subgroup and treatment-by-subgroup interaction.

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DE.T.2.9.2 - Best percent change in the sum of the diameter of measurable tumors based on BICR - Analysis of continuous endpoints - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd			TPC			Difference of LSMeans (95% CI)	P-value	Hedges' g (95% CI)	Interaction P-value [b]
	Nsub	Mean (SD)	LSMean (95% CI) [a]	Nsub	Mean (SD)	LSMean (95% CI) [a]				
Region										0.0242
Asia	137	-43.0(33.07)	-42.58 (-47.77, -37.39)	60	-4.3(27.92)	-5.28 (-13.13, 2.58)	-37.30 (-46.74, -27.87)	<0.0001	-1.20 (-1.52, -0.87)	
North America	54	-37.5(38.82)	-37.25 (-46.70, -27.80)	22	-19.0(27.45)	-19.47 (-34.28, -4.66)	-17.78 (-35.35, -0.20)	0.0474	-0.50 (-1.00, 0.01)	
Europe + Israel	157	-40.3(33.47)	-40.25 (-45.37, -35.12)	74	-19.0(31.26)	-19.13 (-26.59, -11.67)	-21.12 (-30.17, -12.07)	<0.0001	-0.64 (-0.93, -0.36)	
ECOG PS										0.5516
0	191	-41.9(34.34)	-41.74 (-46.49, -36.99)	83	-12.3(31.48)	-12.64 (-19.85, -5.42)	-29.10 (-37.75, -20.45)	<0.0001	-0.87 (-1.13, -0.60)	
1	157	-39.8(34.00)	-39.62 (-44.56, -34.68)	73	-14.5(28.80)	-14.83 (-22.08, -7.58)	-24.79 (-33.57, -16.02)	<0.0001	-0.78 (-1.07, -0.50)	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category;

[a] LSMean obtained from a linear model adjusting for treatment and baseline value.

[b] Two-sided interaction p-value is for the interaction term from a linear model adjusting for treatment, baseline value, subgroup and treatment-by-subgroup interaction.

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Subgroup	T-DXd			TPC			Difference of LSMeans (95% CI)	P-value	Hedges' g (95% CI)	Interaction P-value [b]
	Nsub	Mean (SD)	LSMean (95% CI) [a]	Nsub	Mean (SD)	LSMean (95% CI) [a]				
Number of lines of endocrine therapy received in the metastatic setting										0.7424
0	55	-35.4(30.59)	-35.11 (-43.03, -27.20)	28	-8.0(32.28)	-8.67 (-19.77, 2.43)	-26.44 (-40.08, -12.81)	0.0001	-0.87 (-1.35, -0.40)	
1	98	-47.1(33.73)	-46.98 (-53.63, -40.33)	42	-24.6(33.47)	-24.91 (-35.07, -14.75)	-22.07 (-34.22, -9.92)	0.0004	-0.65 (-1.02, -0.28)	
2	109	-41.6(35.48)	-41.44 (-47.78, -35.11)	46	-13.3(28.57)	-13.65 (-23.44, -3.86)	-27.80 (-39.50, -16.09)	<0.0001	-0.82 (-1.17, -0.46)	
>=3	86	-36.6(34.44)	-36.63 (-43.11, -30.16)	40	-5.3(23.58)	-5.11 (-14.60, 4.38)	-31.52 (-43.02, -20.03)	<0.0001	-1.02 (-1.42, -0.63)	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category;

[a] LSMean obtained from a linear model adjusting for treatment and baseline value.

[b] Two-sided interaction p-value is for the interaction term from a linear model adjusting for treatment, baseline value, subgroup and treatment-by-subgroup interaction.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Subgroup	T-DXd			TPC			Difference of LSMeans (95% CI)	P-value	Hedges' g (95% CI)	Interaction P-value [b]
	Nsub	Mean (SD)	LSMean (95% CI) [a]	Nsub	Mean (SD)	LSMean (95% CI) [a]				
Best Response to last prior cancer systemic therapy										0.1542
PD	161	-38.0(35.50)	-37.84 (-43.13, -32.55)	70	-14.6(31.85)	-14.85 (-22.87, -6.82)	-22.99 (-32.60, -13.37)	<0.0001	-0.67 (-0.96, -0.38)	
PR	46	-49.7(27.80)	-48.61 (-56.76, -40.46)	19	-5.5(30.73)	-8.04 (-20.86, 4.78)	-40.57 (-55.92, -25.21)	<0.0001	-1.42 (-2.00, -0.83)	
SD	78	-39.9(30.33)	-39.85 (-46.27, -33.43)	48	-11.0(27.45)	-11.05 (-19.24, -2.87)	-28.80 (-39.20, -18.39)	<0.0001	-0.99 (-1.37, -0.61)	
Reported history of CNS metastases										0.2636
Yes	35	-40.7(35.68)	-40.18 (-51.25, -29.11)	12	-0.1(24.32)	-1.56 (-20.61, 17.50)	-38.63 (-60.80, -16.45)	0.0006	-1.13 (-1.83, -0.44)	
No	313	-41.0(34.03)	-40.80 (-44.41, -37.18)	144	-14.4(30.43)	-14.79 (-20.12, -9.46)	-26.00 (-32.44, -19.56)	<0.0001	-0.80 (-1.00, -0.59)	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category;

[a] LSMean obtained from a linear model adjusting for treatment and baseline value.

[b] Two-sided interaction p-value is for the interaction term from a linear model adjusting for treatment, baseline value, subgroup and treatment-by-subgroup interaction.

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Subgroup	T-DXd			TPC			Difference of LSMeans (95% CI)	P-value	Hedges' g (95% CI)	Interaction P-value [b]
	Nsub	Mean (SD)	LSMean (95% CI) [a]	Nsub	Mean (SD)	LSMean (95% CI) [a]				
Baseline CNS metastases										0.5010
Yes	22	-38.4(32.03)	-36.86 (-49.94, -23.77)	7	-16.3(30.72)	-21.02 (-44.75, 2.70)	-15.84 (-43.35, 11.68)	0.2594	-0.49 (-1.35, 0.37)	
No	326	-41.1(34.33)	-40.95 (-44.51, -37.39)	149	-13.2(30.26)	-13.52 (-18.79, -8.25)	-27.43 (-33.79, -21.07)	<0.0001	-0.83 (-1.04, -0.63)	
Renal function at baseline										0.2381
Normal Function	188	-40.6(34.95)	-40.65 (-45.44, -35.85)	74	-14.5(30.98)	-14.31 (-21.95, -6.66)	-26.34 (-35.36, -17.32)	<0.0001	-0.78 (-1.06, -0.51)	
Mild Impairment	115	-41.3(32.65)	-40.89 (-46.53, -35.24)	58	-9.7(28.85)	-10.60 (-18.57, -2.64)	-30.29 (-40.07, -20.50)	<0.0001	-0.98 (-1.31, -0.64)	
Moderate Impairment	40	-40.4(36.20)	-39.78 (-50.67, -28.89)	20	-23.6(30.21)	-24.84 (-40.50, -9.19)	-14.93 (-34.42, 4.55)	0.1331	-0.42 (-0.96, 0.12)	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category;

[a] LSMean obtained from a linear model adjusting for treatment and baseline value.

[b] Two-sided interaction p-value is for the interaction term from a linear model adjusting for treatment, baseline value, subgroup and treatment-by-subgroup interaction.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Subgroup	T-DXd			TPC			Difference of LSMeans (95% CI)	P-value	Hedges' g (95% CI)	Interaction P-value [b]
	Nsub	Mean (SD)	LSMean (95% CI) [a]	Nsub	Mean (SD)	LSMean (95% CI) [a]				
Hepatic function at baseline										0.9589
Normal Function	162	-41.8(34.12)	-41.28 (-46.26, -36.30)	80	-14.4(30.66)	-15.44 (-22.54, -8.34)	-25.84 (-34.54, -17.15)	<0.0001	-0.80 (-1.07, -0.52)	
Mild Impairment	182	-39.8(34.39)	-39.75 (-44.54, -34.95)	74	-13.3(29.49)	-13.51 (-21.03, -5.99)	-26.23 (-35.16, -17.31)	<0.0001	-0.79 (-1.07, -0.51)	
Baseline visceral disease										0.0353
Yes	314	-40.1(34.17)	-39.91 (-43.55, -36.26)	136	-15.0(30.79)	-15.33 (-20.87, -9.80)	-24.57 (-31.20, -17.94)	<0.0001	-0.74 (-0.95, -0.54)	
No	34	-48.9(33.40)	-47.83 (-57.68, -37.97)	20	-2.2(23.36)	-4.09 (-16.99, 8.81)	-43.74 (-60.08, -27.40)	<0.0001	-1.47 (-2.09, -0.85)	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category;

[a] LSMean obtained from a linear model adjusting for treatment and baseline value.

[b] Two-sided interaction p-value is for the interaction term from a linear model adjusting for treatment, baseline value, subgroup and treatment-by-subgroup interaction.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:13; Program name: T2\_BCHG\_BICR\_2\_FAS.sas; Output name: T2\_BCHG\_BICR\_2\_FAS.rtf

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DE.T.2.9.2 - Best percent change in the sum of the diameter of measurable tumors based on BICR - Analysis of continuous endpoints - subgroup analysis - Destiny Breast 04 - DCO  
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Subgroup	T-DXd			TPC			Difference of LSMeans (95% CI)	P-value	Hedges' g (95% CI)	Interaction P-value [b]
	Nsub	Mean (SD)	LSMean (95% CI) [a]	Nsub	Mean (SD)	LSMean (95% CI) [a]				
Hormon receptor status (IXRS)										0.9146
Yes	310	-41.5(34.36)	-41.32 (-44.96, -37.68)	137	-13.8(29.65)	-14.24 (-19.73, -8.76)	-27.08 (-33.67, -20.49)	<0.0001	-0.83 (-1.03, -0.62)	
No	38	-36.0(32.41)	-36.11 (-46.43, -25.78)	19	-10.2(34.50)	-10.05 (-24.65, 4.56)	-26.06 (-43.95, -8.17)	0.0043	-0.79 (-1.36, -0.22)	
Hormon receptor status (derived)										0.7120
Positive	312	-41.3(34.39)	-41.06 (-44.69, -37.44)	139	-14.0(29.50)	-14.48 (-19.92, -9.04)	-26.58 (-33.13, -20.04)	<0.0001	-0.81 (-1.02, -0.61)	
Negative	36	-38.1(32.34)	-37.96 (-48.65, -27.28)	17	-7.6(35.76)	-7.78 (-23.34, 7.77)	-30.18 (-49.06, -11.31)	0.0017	-0.91 (-1.51, -0.31)	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category;

[a] LSMean obtained from a linear model adjusting for treatment and baseline value.

[b] Two-sided interaction p-value is for the interaction term from a linear model adjusting for treatment, baseline value, subgroup and treatment-by-subgroup interaction.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:13; Program name: T2\_BCHG\_BICR\_2\_FAS.sas; Output name: T2\_BCHG\_BICR\_2\_FAS.rtf

**Anhang 4-G 2.2.3: Klinische Nutzenrate**

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DE.T.2.5.1 - Clinical benefit rate based on BICR - Analysis of dichotomous endpoints - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

	T-DXd (N=373)	TPC (N=184)	T-DXd vs TPC
Number of subjects with events, n (%)	262 (70.2)	62 (33.7)	
95% CI [a]	(65.3, 74.8)	(26.9, 41.0)	
Odds ratio (95% CI) [b]			4.64 (3.18, 6.78)
Relative risk (95% CI) [b]			2.08 (1.68, 2.58)
Absolute risk reduction (95% CI) [b]			36.55 (27.88, 45.21)
p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value based on the Cochran-Mantel-Haenszel test adjusted for randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 16SEP2022 – 17:01; Program name: T2\_ORR\_BICR\_1\_FAS.sas; Output name: T2\_CBR\_BICR\_1\_FAS.rtf

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DE.T.2.5.2 - Clinical benefit rate based on BICR - Analysis of dichotomous endpoints - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction p-value [d]
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	
HER2 status								0.9952
HER2 IHC 1+	214	150 (70.1) (63.5, 76.1)	107	36 (33.6) (24.8, 43.4)	4.62 (2.81, 7.59)	2.08 (1.57, 2.76)	36.45 (24.90, 48.00)	<0.0001
HER2 IHC 2+/ISH Negative	159	112 (70.4) (62.7, 77.4)	77	26 (33.8) (23.4, 45.4)	4.67 (2.61, 8.37)	2.09 (1.50, 2.90)	36.67 (22.99, 50.36)	<0.0001
Number of prior lines of chemotherapy in a metastatic setting								0.5750
1	221	156 (70.6) (64.1, 76.5)	100	36 (36.0) (26.6, 46.2)	4.27 (2.59, 7.04)	1.96 (1.49, 2.58)	34.59 (22.70, 46.48)	<0.0001
>=2	151	105 (69.5) (61.5, 76.8)	83	26 (31.3) (21.6, 42.4)	5.00 (2.80, 8.93)	2.22 (1.59, 3.10)	38.21 (24.89, 51.53)	<0.0001

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction	
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)		p-value [c]
Prior CDK4/6									0.7044
Yes	235	162 (68.9) (62.6, 74.8)	118	38 (32.2) (23.9, 41.4)	4.67 (2.91, 7.51)	2.14 (1.63, 2.82)	36.73 (25.80, 47.67)	<0.0001	
No	98	76 (77.6) (68.0, 85.4)	48	19 (39.6) (25.8, 54.7)	5.27 (2.50, 11.14)	1.96 (1.36, 2.82)	37.97 (20.30, 55.63)	<0.0001	
Age									0.0331
<65	290	205 (70.7) (65.1, 75.9)	136	40 (29.4) (21.9, 37.8)	5.79 (3.70, 9.05)	2.40 (1.83, 3.15)	41.28 (31.46, 51.10)	<0.0001	
>=65	83	57 (68.7) (57.6, 78.4)	48	22 (45.8) (31.4, 60.8)	2.59 (1.24, 5.39)	1.50 (1.07, 2.11)	22.84 (3.93, 41.76)	0.0103	

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction p-value [d]
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	
Age								0.0217
<75	359	252 (70.2) (65.2, 74.9)	175	56 (32.0) (25.2, 39.5)	5.00 (3.39, 7.39)	2.19 (1.75, 2.75)	38.19 (29.39, 47.00)	<0.0001
>=75	14	10 (71.4) (41.9, 91.6)	9	6 (66.7) (29.9, 92.5)	1.25 (0.21, 7.62)	1.07 (0.61, 1.89)	4.76 (-43.20, 52.73)	0.8127
Race								0.8691
White	176	122 (69.3) (61.9, 76.0)	91	31 (34.1) (24.5, 44.7)	4.37 (2.55, 7.50)	2.03 (1.50, 2.75)	35.25 (22.53, 47.97)	<0.0001
Non-White	197	140 (71.1) (64.2, 77.3)	92	31 (33.7) (24.2, 44.3)	4.83 (2.84, 8.22)	2.11 (1.56, 2.85)	37.37 (25.02, 49.72)	<0.0001

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.



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DE.T.2.5.2 - Clinical benefit rate based on BICR - Analysis of dichotomous endpoints - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction p-value [d]
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	
Region								0.7694
Asia	147	108 (73.5) (65.6, 80.4)	66	21 (31.8) (20.9, 44.4)	5.93 (3.15, 11.19)	2.31 (1.60, 3.33)	41.65 (27.24, 56.06)	<0.0001
North America	60	36 (60.0) (46.5, 72.4)	33	10 (30.3) (15.6, 48.7)	3.45 (1.40, 8.52)	1.98 (1.13, 3.46)	29.70 (7.36, 52.03)	0.0064
Europe + Israel	166	118 (71.1) (63.6, 77.8)	85	31 (36.5) (26.3, 47.6)	4.28 (2.46, 7.46)	1.95 (1.45, 2.62)	34.61 (21.38, 47.84)	<0.0001
ECOG PS								0.3353
0	200	144 (72.0) (65.2, 78.1)	105	33 (31.4) (22.7, 41.2)	5.61 (3.35, 9.39)	2.29 (1.70, 3.08)	40.57 (29.00, 52.14)	<0.0001
1	173	118 (68.2) (60.7, 75.1)	79	29 (36.7) (26.1, 48.3)	3.70 (2.12, 6.46)	1.86 (1.37, 2.53)	31.50 (17.88, 45.11)	<0.0001

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction p-value [d]
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	
Number of lines of endocrine therapy received in the metastatic setting								0.3945
0	60	39 (65.0) (51.6, 76.9)	34	11 (32.4) (17.4, 50.5)	3.88 (1.59, 9.49)	2.01 (1.19, 3.38)	32.65 (10.52, 54.77)	0.0024
1	108	76 (70.4) (60.8, 78.8)	51	22 (43.1) (29.3, 57.8)	3.13 (1.57, 6.25)	1.63 (1.16, 2.29)	27.23 (9.70, 44.77)	0.0010
2	115	81 (70.4) (61.2, 78.6)	54	15 (27.8) (16.5, 41.6)	6.19 (3.02, 12.70)	2.54 (1.62, 3.96)	42.66 (26.73, 58.59)	<0.0001
>=3	90	66 (73.3) (63.0, 82.1)	45	14 (31.1) (18.2, 46.6)	6.09 (2.78, 13.35)	2.36 (1.50, 3.71)	42.22 (24.23, 60.21)	<0.0001

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

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DE.T.2.5.2 - Clinical benefit rate based on BICR - Analysis of dichotomous endpoints - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction p-value [d]
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	
Best Response to last prior cancer systemic therapy								0.0260
PD	174	117 (67.2) (59.7, 74.2)	85	26 (30.6) (21.0, 41.5)	4.66 (2.66, 8.15)	2.20 (1.57, 3.08)	36.65 (23.75, 49.55)	<0.0001
PR	48	37 (77.1) (62.7, 88.0)	22	3 (13.6) (2.9, 34.9)	21.30 (5.30, 85.64)	5.65 (1.95, 16.36)	63.45 (41.50, 85.39)	<0.0001
SD	82	57 (69.5) (58.4, 79.2)	55	26 (47.3) (33.7, 61.2)	2.54 (1.25, 5.16)	1.47 (1.07, 2.01)	22.24 (4.19, 40.29)	0.0093
Reported history of CNS metastases								0.7987
Yes	37	23 (62.2) (44.8, 77.5)	15	4 (26.7) (7.8, 55.1)	4.52 (1.20, 16.97)	2.33 (0.97, 5.60)	35.50 (3.52, 67.48)	0.0215
No	336	239 (71.1) (66.0, 75.9)	169	58 (34.3) (27.2, 42.0)	4.72 (3.17, 7.00)	2.07 (1.66, 2.58)	36.81 (27.72, 45.90)	<0.0001

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC				Interaction p-value [d]
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	p-value [c]	
Baseline CNS metastases									0.1797
Yes	24	15 (62.5) (40.6, 81.2)	8	4 (50.0) (15.7, 84.3)	1.67 (0.33, 8.37)	1.25 (0.59, 2.67)	12.50 (-35.53, 60.53)	0.5395	
No	349	247 (70.8) (65.7, 75.5)	176	58 (33.0) (26.1, 40.4)	4.93 (3.34, 7.28)	2.15 (1.72, 2.68)	37.82 (28.97, 46.67)	<0.0001	
Renal function at baseline									0.0012
Normal Function	202	140 (69.3) (62.4, 75.6)	87	22 (25.3) (16.6, 35.7)	6.67 (3.78, 11.78)	2.74 (1.89, 3.98)	44.02 (32.07, 55.97)	<0.0001	
Mild Impairment	123	90 (73.2) (64.4, 80.8)	69	24 (34.8) (23.7, 47.2)	5.11 (2.71, 9.66)	2.10 (1.50, 2.96)	38.39 (23.56, 53.22)	<0.0001	
Moderate Impairment	41	29 (70.7) (54.5, 83.9)	23	15 (65.2) (42.7, 83.6)	1.29 (0.43, 3.83)	1.08 (0.76, 1.55)	5.51 (-21.81, 32.84)	0.6505	

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction p-value [d]
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	
Hepatic function at baseline								
Normal Function	170	131 (77.1) (70.0, 83.1)	98	37 (37.8) (28.2, 48.1)	5.54 (3.22, 9.53)	2.04 (1.56, 2.67)	39.30 (27.01, 51.60)	<0.0001
Mild Impairment	195	129 (66.2) (59.0, 72.8)	84	25 (29.8) (20.3, 40.7)	4.61 (2.65, 8.03)	2.22 (1.58, 3.13)	36.39 (23.72, 49.06)	<0.0001
Baseline visceral disease								
Yes	332	232 (69.9) (64.6, 74.8)	157	57 (36.3) (28.8, 44.3)	4.07 (2.73, 6.08)	1.92 (1.55, 2.40)	33.57 (24.11, 43.04)	<0.0001
No	41	30 (73.2) (57.1, 85.8)	27	5 (18.5) (6.3, 38.1)	12.00 (3.64, 39.51)	3.95 (1.75, 8.91)	54.65 (31.62, 77.69)	<0.0001

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction p-value [d]
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	
Hormon receptor status (IXRS)								0.7176
Positive	331	238 (71.9) (66.7, 76.7)	163	57 (35.0) (27.7, 42.8)	4.76 (3.19, 7.11)	2.06 (1.65, 2.56)	36.93 (27.70, 46.17)	<0.0001
Negative	42	24 (57.1) (41.0, 72.3)	21	5 (23.8) (8.2, 47.2)	4.27 (1.32, 13.82)	2.40 (1.07, 5.39)	33.33 (6.19, 60.48)	0.0131
Hormon receptor status (derived)								0.8432
Positive	333	237 (71.2) (66.0, 76.0)	166	57 (34.3) (27.2, 42.1)	4.72 (3.17, 7.03)	2.07 (1.66, 2.59)	36.83 (27.67, 45.99)	<0.0001
Negative	40	25 (62.5) (45.8, 77.3)	18	5 (27.8) (9.7, 53.5)	4.33 (1.29, 14.59)	2.25 (1.03, 4.92)	34.72 (5.14, 64.31)	0.0152

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

**Anhang 4-G 2.2.4: Klinische Kontrollrate**

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	T-DXd (N=373)	TPC (N=184)	T-DXd vs TPC
Number of subjects with events, n (%)	325 (87.1)	121 (65.8)	
95% CI [a]	(83.3, 90.4)	(58.4, 72.6)	
Odds ratio (95% CI) [b]			3.53 (2.29, 5.42)
Relative risk (95% CI) [b]			1.32 (1.19, 1.48)
Absolute risk reduction (95% CI) [b]			21.37 (13.31, 29.43)
p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value based on the Cochran-Mantel-Haenszel test adjusted for randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 16SEP2022 – 17:01; Program name: T2\_ORR\_BICR\_1\_FAS.sas; Output name: T2\_DCR\_BICR\_1\_FAS.rtf



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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction p-value [d]
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	
HER2 status								0.2122
HER2 IHC 1+	214	182 (85.0) (79.6, 89.5)	107	73 (68.2) (58.5, 76.9)	2.65 (1.52, 4.61)	1.25 (1.08, 1.44)	16.82 (6.09, 27.56)	0.0004
HER2 IHC 2+/ISH Negative	159	143 (89.9) (84.2, 94.1)	77	48 (62.3) (50.6, 73.1)	5.40 (2.70, 10.79)	1.44 (1.20, 1.73)	27.60 (14.85, 40.35)	<0.0001
Number of prior lines of chemotherapy in a metastatic setting								0.5791
1	221	195 (88.2) (83.2, 92.2)	100	69 (69.0) (59.0, 77.9)	3.37 (1.87, 6.07)	1.28 (1.11, 1.47)	19.24 (8.50, 29.97)	<0.0001
>=2	151	129 (85.4) (78.8, 90.6)	83	52 (62.7) (51.3, 73.0)	3.50 (1.85, 6.59)	1.36 (1.14, 1.63)	22.78 (10.02, 35.54)	<0.0001

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction p-value [d]
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	
Prior CDK4/6								0.4073
Yes	235	203 (86.4) (81.3, 90.5)	118	79 (66.9) (57.7, 75.3)	3.13 (1.83, 5.35)	1.29 (1.13, 1.48)	19.43 (9.24, 29.62)	<0.0001
No	98	91 (92.9) (85.8, 97.1)	48	31 (64.6) (49.5, 77.8)	7.13 (2.70, 18.81)	1.44 (1.16, 1.79)	28.27 (12.26, 44.28)	<0.0001
Age								0.0175
<65	290	253 (87.2) (82.8, 90.9)	136	83 (61.0) (52.3, 69.3)	4.37 (2.68, 7.11)	1.43 (1.24, 1.65)	26.21 (16.62, 35.80)	<0.0001
>=65	83	72 (86.7) (77.5, 93.2)	48	38 (79.2) (65.0, 89.5)	1.72 (0.67, 4.42)	1.10 (0.93, 1.30)	7.58 (-7.67, 22.83)	0.2564

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction p-value [d]
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	
Age								<.0001
<75	359	312 (86.9) (83.0, 90.2)	175	112 (64.0) (56.4, 71.1)	3.73 (2.42, 5.77)	1.36 (1.21, 1.53)	22.91 (14.56, 31.25)	<0.0001
>=75	14	13 (92.9) (66.1, 99.8)	9	9 (100.0) (66.4, 100.0)	NE (NE, NE)	0.93 (0.80, 1.07)	-7.14 (-29.76, 15.47)	0.4227
Race								0.4290
White	176	151 (85.8) (79.7, 90.6)	91	62 (68.1) (57.5, 77.5)	2.83 (1.53, 5.21)	1.26 (1.08, 1.47)	17.66 (5.96, 29.37)	0.0007
Non-White	197	174 (88.3) (83.0, 92.5)	92	59 (64.1) (53.5, 73.9)	4.23 (2.30, 7.78)	1.38 (1.17, 1.62)	24.19 (12.62, 35.77)	<0.0001

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction p-value [d]
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	
Region								0.3075
Asia	147	134 (91.2) (85.4, 95.2)	66	41 (62.1) (49.3, 73.8)	6.29 (2.95, 13.39)	1.47 (1.21, 1.78)	29.04 (15.37, 42.70)	<0.0001
North America	60	49 (81.7) (69.6, 90.5)	33	20 (60.6) (42.1, 77.1)	2.90 (1.11, 7.54)	1.35 (1.00, 1.82)	21.06 (-0.62, 42.74)	0.0272
Europe + Israel	166	142 (85.5) (79.3, 90.5)	85	60 (70.6) (59.7, 80.0)	2.47 (1.30, 4.66)	1.21 (1.04, 1.41)	14.95 (3.00, 26.91)	0.0048
ECOG PS								0.0670
0	200	180 (90.0) (85.0, 93.8)	105	65 (61.9) (51.9, 71.2)	5.54 (3.02, 10.16)	1.45 (1.24, 1.70)	28.10 (17.19, 39.00)	<0.0001
1	173	145 (83.8) (77.5, 89.0)	79	56 (70.9) (59.6, 80.6)	2.13 (1.13, 4.00)	1.18 (1.01, 1.38)	12.93 (0.58, 25.27)	0.0180

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction p-value [d]
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	
Number of lines of endocrine therapy received in the metastatic setting								0.3269
0	60	50 (83.3) (71.5, 91.7)	34	18 (52.9) (35.1, 70.2)	4.44 (1.71, 11.56)	1.57 (1.12, 2.20)	30.39 (8.84, 51.94)	0.0016
1	108	93 (86.1) (78.1, 92.0)	51	38 (74.5) (60.4, 85.7)	2.12 (0.92, 4.88)	1.16 (0.97, 1.38)	11.60 (-3.47, 26.67)	0.0739
2	115	100 (87.0) (79.4, 92.5)	54	36 (66.7) (52.5, 78.9)	3.33 (1.52, 7.30)	1.30 (1.07, 1.60)	20.29 (4.93, 35.65)	0.0020
>=3	90	82 (91.1) (83.2, 96.1)	45	29 (64.4) (48.8, 78.1)	5.66 (2.19, 14.60)	1.41 (1.13, 1.77)	26.67 (9.83, 43.50)	0.0001

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction p-value [d]
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	
Best Response to last prior cancer systemic therapy								0.2720
PD	174	146 (83.9) (77.6, 89.0)	85	56 (65.9) (54.8, 75.8)	2.70 (1.48, 4.94)	1.27 (1.08, 1.50)	18.03 (5.69, 30.36)	0.0010
PR	48	47 (97.9) (88.9, 99.9)	22	12 (54.5) (32.2, 75.6)	39.17 (4.56, 336.63)	1.80 (1.22, 2.63)	43.37 (18.86, 67.88)	<0.0001
SD	82	75 (91.5) (83.2, 96.5)	55	38 (69.1) (55.2, 80.9)	4.79 (1.83, 12.55)	1.32 (1.10, 1.60)	22.37 (7.23, 37.52)	0.0008
Reported history of CNS metastases								0.3240
Yes	37	30 (81.1) (64.8, 92.0)	15	7 (46.7) (21.3, 73.4)	4.90 (1.33, 18.08)	1.74 (0.99, 3.05)	34.41 (1.50, 67.32)	0.0140
No	336	295 (87.8) (83.8, 91.1)	169	114 (67.5) (59.8, 74.5)	3.47 (2.19, 5.49)	1.30 (1.16, 1.46)	20.34 (12.01, 28.67)	<0.0001

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction p-value [d]
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	
Baseline CNS metastases								0.4224
Yes	24	20 (83.3) (62.6, 95.3)	8	6 (75.0) (34.9, 96.8)	1.67 (0.24, 11.45)	1.11 (0.72, 1.72)	8.33 (-33.51, 50.17)	0.6067
No	349	305 (87.4) (83.4, 90.7)	176	115 (65.3) (57.8, 72.3)	3.68 (2.36, 5.73)	1.34 (1.19, 1.50)	22.05 (13.78, 30.32)	<0.0001
Renal function at baseline								0.0109
Normal Function	202	172 (85.1) (79.5, 89.8)	87	52 (59.8) (48.7, 70.1)	3.86 (2.17, 6.88)	1.42 (1.19, 1.71)	25.38 (13.14, 37.61)	<0.0001
Mild Impairment	123	110 (89.4) (82.6, 94.3)	69	47 (68.1) (55.8, 78.8)	3.96 (1.84, 8.52)	1.31 (1.10, 1.56)	21.31 (7.92, 34.71)	0.0003
Moderate Impairment	41	38 (92.7) (80.1, 98.5)	23	21 (91.3) (72.0, 98.9)	1.21 (0.19, 7.80)	1.02 (0.87, 1.18)	1.38 (-16.02, 18.78)	0.8449

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction p-value [d]
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	
Hepatic function at baseline								
Normal Function	170	159 (93.5) (88.7, 96.7)	98	69 (70.4) (60.3, 79.2)	6.08 (2.87, 12.85)	1.33 (1.16, 1.52)	23.12 (12.55, 33.69)	<0.0001
Mild Impairment	195	162 (83.1) (77.1, 88.1)	84	52 (61.9) (50.7, 72.3)	3.02 (1.69, 5.38)	1.34 (1.12, 1.61)	21.17 (8.68, 33.67)	0.0001
Baseline visceral disease								
Yes	332	288 (86.7) (82.6, 90.2)	157	106 (67.5) (59.6, 74.8)	3.15 (1.99, 4.99)	1.28 (1.14, 1.44)	19.23 (10.58, 27.88)	<0.0001
No	41	37 (90.2) (76.9, 97.3)	27	15 (55.6) (35.3, 74.5)	7.40 (2.06, 26.64)	1.62 (1.14, 2.31)	34.69 (10.79, 58.59)	0.0011

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.



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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction p-value [d]
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	
Hormon receptor status (IXRS)								0.9408
Positive	331	291 (87.9) (83.9, 91.2)	163	108 (66.3) (58.4, 73.5)	3.70 (2.33, 5.89)	1.33 (1.18, 1.49)	21.66 (13.14, 30.18)	<0.0001
Negative	42	34 (81.0) (65.9, 91.4)	21	13 (61.9) (38.4, 81.9)	2.62 (0.81, 8.43)	1.31 (0.91, 1.89)	19.05 (-8.45, 46.54)	0.1043
Hormon receptor status (derived)								0.9467
Positive	333	293 (88.0) (84.0, 91.3)	166	110 (66.3) (58.5, 73.4)	3.73 (2.35, 5.91)	1.33 (1.18, 1.49)	21.72 (13.28, 30.17)	<0.0001
Negative	40	32 (80.0) (64.4, 90.9)	18	11 (61.1) (35.7, 82.7)	2.55 (0.75, 8.66)	1.31 (0.88, 1.95)	18.89 (-10.85, 48.62)	0.1319

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

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DE.T.2.6.3 - Disease control rate based on investigator's assessment - Analysis of dichotomous endpoints - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

	T-DXd (N=373)	TPC (N=184)	T-DXd vs TPC
Number of subjects with events, n (%)	328 (87.9)	124 (67.4)	
95% CI [a]	(84.2, 91.1)	(60.1, 74.1)	
Odds ratio (95% CI) [b]			3.53 (2.28, 5.47)
Relative risk (95% CI) [b]			1.30 (1.17, 1.45)
Absolute risk reduction (95% CI) [b]			20.54 (12.60, 28.49)
p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value based on the Cochran-Mantel-Haenszel test adjusted for randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 16SEP2022 – 17:01; Program name: T2\_ORR\_BICR\_1\_FAS.sas; Output name: T2\_DCR\_INVE\_3\_FAS.rtf

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction p-value [d]
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	
HER2 status								0.7837
HER2 IHC 1+	214	185 (86.4) (81.1, 90.7)	107	70 (65.4) (55.6, 74.4)	3.37 (1.93, 5.89)	1.32 (1.14, 1.53)	21.03 (10.22, 31.84)	<0.0001
HER2 IHC 2+/ISH Negative	159	143 (89.9) (84.2, 94.1)	77	54 (70.1) (58.6, 80.0)	3.81 (1.87, 7.75)	1.28 (1.10, 1.50)	19.81 (7.60, 32.01)	0.0001
Number of prior lines of chemotherapy in a metastatic setting								0.2256
1	221	197 (89.1) (84.3, 92.9)	100	73 (73.0) (63.2, 81.4)	3.04 (1.65, 5.60)	1.22 (1.07, 1.39)	16.14 (5.79, 26.49)	0.0003
>=2	151	130 (86.1) (79.5, 91.2)	83	51 (61.4) (50.1, 71.9)	3.88 (2.05, 7.36)	1.40 (1.17, 1.68)	24.65 (11.88, 37.42)	<0.0001

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction p-value [d]
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	
Prior CDK4/6								0.7983
Yes	235	201 (85.5) (80.4, 89.8)	118	79 (66.9) (57.7, 75.3)	2.92 (1.72, 4.95)	1.28 (1.11, 1.47)	18.58 (8.34, 28.82)	<0.0001
No	98	94 (95.9) (89.9, 98.9)	48	35 (72.9) (58.2, 84.7)	8.73 (2.67, 28.58)	1.32 (1.10, 1.57)	23.00 (8.28, 37.72)	<0.0001
Age								0.1974
<65	290	255 (87.9) (83.6, 91.4)	136	88 (64.7) (56.1, 72.7)	3.97 (2.41, 6.54)	1.36 (1.19, 1.55)	23.23 (13.82, 32.63)	<0.0001
>=65	83	73 (88.0) (79.0, 94.1)	48	36 (75.0) (60.4, 86.4)	2.43 (0.96, 6.16)	1.17 (0.98, 1.41)	12.95 (-2.80, 28.71)	0.0570

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction p-value [d]
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	
Age								0.0001
<75	359	315 (87.7) (83.9, 91.0)	175	115 (65.7) (58.2, 72.7)	3.74 (2.40, 5.82)	1.34 (1.19, 1.50)	22.03 (13.80, 30.26)	<0.0001
>=75	14	13 (92.9) (66.1, 99.8)	9	9 (100.0) (66.4, 100.0)	NE (NE, NE)	0.93 (0.80, 1.07)	-7.14 (-29.76, 15.47)	0.4227
Race								0.6831
White	176	148 (84.1) (77.8, 89.2)	91	60 (65.9) (55.3, 75.5)	2.73 (1.51, 4.94)	1.28 (1.09, 1.50)	18.16 (6.19, 30.13)	0.0007
Non-White	197	180 (91.4) (86.5, 94.9)	92	63 (68.5) (58.0, 77.8)	4.87 (2.51, 9.47)	1.33 (1.15, 1.54)	22.89 (11.82, 33.96)	<0.0001

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

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DE.T.2.6.4 - Disease control rate based on investigator's assessment - Analysis of dichotomous endpoints - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction p-value [d]
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	
<b>Region</b>								
Asia	147	138 (93.9) (88.7, 97.2)	66	45 (68.2) (55.6, 79.1)	7.16 (3.06, 16.75)	1.38 (1.16, 1.63)	25.70 (12.71, 38.68)	<0.0001
North America	60	49 (81.7) (69.6, 90.5)	33	17 (51.5) (33.5, 69.2)	4.19 (1.63, 10.79)	1.59 (1.11, 2.25)	30.15 (8.14, 52.16)	0.0023
Europe + Israel	166	141 (84.9) (78.6, 90.0)	85	62 (72.9) (62.2, 82.0)	2.09 (1.10, 3.97)	1.16 (1.01, 1.35)	12.00 (0.21, 23.79)	0.0224
<b>ECOG PS</b>								
0	200	181 (90.5) (85.6, 94.2)	105	66 (62.9) (52.9, 72.1)	5.63 (3.04, 10.43)	1.44 (1.23, 1.68)	27.64 (16.82, 38.47)	<0.0001
1	173	147 (85.0) (78.8, 89.9)	79	58 (73.4) (62.3, 82.7)	2.05 (1.07, 3.92)	1.16 (1.00, 1.34)	11.55 (-0.47, 23.58)	0.0293

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction p-value [d]
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	
Number of lines of endocrine therapy received in the metastatic setting								0.1063
0	60	51 (85.0) (73.4, 92.9)	34	19 (55.9) (37.9, 72.8)	4.47 (1.68, 11.92)	1.52 (1.11, 2.09)	29.12 (7.84, 50.40)	0.0020
1	108	95 (88.0) (80.3, 93.4)	51	41 (80.4) (66.9, 90.2)	1.78 (0.72, 4.39)	1.09 (0.94, 1.27)	7.57 (-6.38, 21.52)	0.2067
2	115	101 (87.8) (80.4, 93.2)	54	36 (66.7) (52.5, 78.9)	3.61 (1.63, 7.99)	1.32 (1.08, 1.61)	21.16 (5.88, 36.44)	0.0011
>=3	90	81 (90.0) (81.9, 95.3)	45	28 (62.2) (46.5, 76.2)	5.46 (2.19, 13.64)	1.45 (1.14, 1.83)	27.78 (10.65, 44.91)	0.0001

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction p-value [d]
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	
Best Response to last prior cancer systemic therapy								0.2239
PD	174	150 (86.2) (80.2, 91.0)	85	52 (61.2) (50.0, 71.6)	3.97 (2.15, 7.32)	1.41 (1.18, 1.69)	25.03 (12.60, 37.46)	<0.0001
PR	48	45 (93.8) (82.8, 98.7)	22	15 (68.2) (45.1, 86.1)	7.00 (1.60, 30.55)	1.37 (1.02, 1.85)	25.57 (1.62, 49.52)	0.0048
SD	82	74 (90.2) (81.7, 95.7)	55	43 (78.2) (65.0, 88.2)	2.58 (0.98, 6.81)	1.15 (0.99, 1.35)	12.06 (-2.12, 26.25)	0.0508
Reported history of CNS metastases								0.2408
Yes	37	31 (83.8) (68.0, 93.8)	15	7 (46.7) (21.3, 73.4)	5.90 (1.55, 22.53)	1.80 (1.03, 3.14)	37.12 (4.53, 69.70)	0.0068
No	336	297 (88.4) (84.5, 91.6)	169	117 (69.2) (61.7, 76.1)	3.38 (2.12, 5.40)	1.28 (1.15, 1.42)	19.16 (10.96, 27.36)	<0.0001

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction p-value [d]
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	
Baseline CNS metastases								0.9423
Yes	24	20 (83.3) (62.6, 95.3)	8	5 (62.5) (24.5, 91.5)	3.00 (0.50, 17.95)	1.33 (0.76, 2.35)	20.83 (-24.21, 65.88)	0.2244
No	349	308 (88.3) (84.4, 91.4)	176	119 (67.6) (60.2, 74.5)	3.60 (2.29, 5.66)	1.31 (1.17, 1.46)	20.64 (12.52, 28.76)	<0.0001
Renal function at baseline								0.0744
Normal Function	202	178 (88.1) (82.8, 92.2)	87	57 (65.5) (54.6, 75.4)	3.90 (2.11, 7.21)	1.34 (1.15, 1.58)	22.60 (10.84, 34.36)	<0.0001
Mild Impairment	123	108 (87.8) (80.7, 93.0)	69	45 (65.2) (52.8, 76.3)	3.84 (1.85, 7.99)	1.35 (1.12, 1.62)	22.59 (8.82, 36.36)	0.0002
Moderate Impairment	41	37 (90.2) (76.9, 97.3)	23	20 (87.0) (66.4, 97.2)	1.39 (0.28, 6.82)	1.04 (0.86, 1.25)	3.29 (-16.60, 23.17)	0.6883

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction p-value [d]
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	
Hepatic function at baseline								
Normal Function	170	160 (94.1) (89.4, 97.1)	98	72 (73.5) (63.6, 81.9)	5.78 (2.65, 12.61)	1.28 (1.13, 1.45)	20.65 (10.41, 30.88)	<0.0001
Mild Impairment	195	164 (84.1) (78.2, 88.9)	84	52 (61.9) (50.7, 72.3)	3.26 (1.82, 5.84)	1.36 (1.14, 1.62)	22.20 (9.76, 34.63)	<0.0001
Baseline visceral disease								
Yes	332	290 (87.3) (83.3, 90.7)	157	108 (68.8) (60.9, 75.9)	3.13 (1.96, 5.00)	1.27 (1.13, 1.42)	18.56 (10.01, 27.11)	<0.0001
No	41	38 (92.7) (80.1, 98.5)	27	16 (59.3) (38.8, 77.6)	8.71 (2.14, 35.45)	1.56 (1.13, 2.16)	33.42 (10.18, 56.67)	0.0009

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

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Subgroup	T-DXd (N=373)		TPC (N=184)		T-DXd vs TPC			Interaction p-value [d]
	Nsub	No. of subjects with events n (%) (95% CI) [a]	Nsub	No. of subjects with events n (%) (95% CI) [a]	OR [b] (95% CI)	RR [b] (95% CI)	ARR [b] (95% CI)	
Hormon receptor status (IXRS)								0.9251
Positive	331	292 (88.2) (84.2, 91.5)	163	110 (67.5) (59.7, 74.6)	3.61 (2.26, 5.76)	1.31 (1.17, 1.46)	20.73 (12.29, 29.18)	<0.0001
Negative	42	36 (85.7) (71.5, 94.6)	21	14 (66.7) (43.0, 85.4)	3.00 (0.86, 10.50)	1.29 (0.93, 1.78)	19.05 (-7.29, 45.39)	0.0806
Hormon receptor status (derived)								0.4453
Positive	333	294 (88.3) (84.3, 91.5)	166	114 (68.7) (61.0, 75.6)	3.44 (2.15, 5.49)	1.29 (1.15, 1.43)	19.61 (11.31, 27.92)	<0.0001
Negative	40	34 (85.0) (70.2, 94.3)	18	10 (55.6) (30.8, 78.5)	4.53 (1.27, 16.17)	1.53 (0.99, 2.36)	29.44 (-0.07, 58.96)	0.0162

N: number of subjects in analysis set; Nsub: number of number of subjects in subgroup category; %: proportion of subjects in subgroup category; OR: odds ratio; RR: risk ratio; ARR: absolute risk reduction (presented on percentage point scale).

[a] Based on Clopper-Pearson method for single proportion.

[b] Derived using the Cochran-Mantel-Haenszel method. Absolute risk reduction is presented on percentage point scale.

[c] Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test

[d] Two-sided p-value from Cochran's Q test for heterogeneity of relative risk.

**Anhang 4-G 2.2.5: Zeit bis zum Ansprechen**

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DE.T.2.7.1 - Time to response based on BICR - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	196 (52.5)	30 (16.3)	
Number of subjects censored, n (%)	177 (47.5)	154 (83.7)	
Median time to first event (months) [a]	5.0	NE	
95% Confidence Interval	[4.2, 5.6]	[7.2, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			2.9392
95% Confidence Interval			[1.9948, 4.3309]
p-value			<0.0001
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
HER2 status										0.2780
HER2 IHC 1+	214	105 (49.1)	109 (50.9)	5.6 (4.2, 9.5)	107	18 (16.8)	89 (83.2)	8.3 (7.1, NE)	2.3708 (1.4349, 3.9172)	0.0005
HER2 IHC 2+/ISH Negative	159	91 (57.2)	68 (42.8)	4.2 (3.2, 5.5)	77	12 (15.6)	65 (84.4)	NE (7.2, NE)	3.5612 (1.9496, 6.5049)	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.2686
1	221	113 (51.1)	108 (48.9)	5.6 (4.2, 7.2)	100	19 (19.0)	81 (81.0)	NE (7.1, NE)	2.3443 (1.4403, 3.8157) 0.0006	0.0004	
>=2	151	82 (54.3)	69 (45.7)	4.2 (3.1, 5.6)	83	11 (13.3)	72 (86.7)	8.3 (7.2, NE)	3.6897 (1.9636, 6.9332) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Prior CDK4/6											0.2694
Yes	235	119 (50.6)	116 (49.4)	5.4 (4.2, 5.7)	118	15 (12.7)	103 (87.3)	NE (NE, NE)	3.4552 (2.0174, 5.9177) <0.0001	<0.0001	
No	98	57 (58.2)	41 (41.8)	4.5 (4.0, 8.5)	48	12 (25.0)	36 (75.0)	8.3 (7.1, NE)	2.1352 (1.1439, 3.9855) 0.0172	0.0148	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Age										0.4338
<65	290	156 (53.8)	134 (46.2)	5.0 (4.1, 5.7)	136	20 (14.7)	116 (85.3)	NE (7.1, NE)	3.1281 (1.9616, 4.9883) <0.0001	<0.0001
>=65	83	40 (48.2)	43 (51.8)	5.4 (4.1, 9.7)	48	10 (20.8)	38 (79.2)	NE (7.2, NE)	2.2715 (1.1337, 4.5512) 0.0207	0.0176

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											
<75	359	189 (52.6)	170 (47.4)	5.4 (4.2, 5.6)	175	27 (15.4)	148 (84.6)	NE (7.2, NE)	2.9376 (1.9608, 4.4009) <0.0001	<0.0001	0.4764
>=75	14	7 (50.0)	7 (50.0)	4.2 (1.5, NE)	9	3 (33.3)	6 (66.7)	7.2 (1.2, NE)	1.8224 (0.4672, 7.1077) 0.3875	0.3897	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Race										0.5045
White	176	95 (54.0)	81 (46.0)	5.4 (4.1, 5.6)	91	16 (17.6)	75 (82.4)	NE (6.9, NE)	2.4377 (1.4324, 4.1487) 0.0010	0.0007
Non-White	197	101 (51.3)	96 (48.7)	4.4 (4.1, 9.6)	92	14 (15.2)	78 (84.8)	NE (7.2, NE)	3.2233 (1.8415, 5.6418) <0.0001	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Region											0.1387
Asia	147	79 (53.7)	68 (46.3)	4.4 (4.0, 7.2)	66	9 (13.6)	57 (86.4)	NE (7.2, NE)	3.6299 (1.8200, 7.2395) 0.0003	<0.0001	
North America	60	26 (43.3)	34 (56.7)	5.5 (3.1, NE)	33	7 (21.2)	26 (78.8)	6.9 (6.9, NE)	1.2992 (0.5608, 3.0100) 0.5415	0.5463	
Europe + Israel	166	91 (54.8)	75 (45.2)	5.4 (3.7, 6.5)	85	14 (16.5)	71 (83.5)	NE (7.1, NE)	3.1196 (1.7741, 5.4854) 0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
ECOG PS											
0	200	110 (55.0)	90 (45.0)	4.5 (4.1, 6.9)	105	17 (16.2)	88 (83.8)	NE (7.2, NE)	2.6556 (1.5912, 4.4319) 0.0002	0.0001	0.7472
1	173	86 (49.7)	87 (50.3)	5.4 (3.1, 6.5)	79	13 (16.5)	66 (83.5)	NE (7.2, NE)	3.0707 (1.7116, 5.5090) 0.0002	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting										0.4753
0	60	29 (48.3)	31 (51.7)	6.5 (3.2, NE)	34	6 (17.6)	28 (82.4)	NE (4.2, NE)	2.0557 (0.8473, 4.9876) 0.1110	0.1024
1	108	61 (56.5)	47 (43.5)	4.1 (2.8, 5.6)	51	10 (19.6)	41 (80.4)	NE (7.1, NE)	3.3162 (1.6977, 6.4774) 0.0004	0.0002
2	115	59 (51.3)	56 (48.7)	5.6 (4.1, 8.4)	54	10 (18.5)	44 (81.5)	8.3 (7.2, NE)	2.1310 (1.0852, 4.1848) 0.0280	0.0246
>=3	90	47 (52.2)	43 (47.8)	4.5 (4.2, 9.6)	45	4 (8.9)	41 (91.1)	7.2 (6.9, NE)	4.5146 (1.6223, 12.5633) 0.0039	0.0015

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.7797
PD	174	88 (50.6)	86 (49.4)	5.4 (4.1, 8.3)	85	14 (16.5)	71 (83.5)	NE (7.1, NE)	2.4413 (1.3846, 4.3042) 0.0020	0.0014
PR	48	31 (64.6)	17 (35.4)	4.2 (2.8, 5.6)	22	3 (13.6)	19 (86.4)	8.3 (4.2, 8.3)	3.9256 (1.1952, 12.8940) 0.0242	0.0149
SD	82	39 (47.6)	43 (52.4)	6.9 (4.2, 13.9)	55	9 (16.4)	46 (83.6)	NE (NE, NE)	2.7875 (1.3490, 5.7603) 0.0056	0.0038

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.2.7.2 - Time to response based on BICR - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.4509
Yes	37	18 (48.6)	19 (51.4)	4.5 (2.8, NE)	15	1 (6.7)	14 (93.3)	NE (NE, NE)	5.4067 (0.7198, 40.6135) 0.1009	0.0656
No	336	178 (53.0)	158 (47.0)	5.4 (4.2, 5.7)	169	29 (17.2)	140 (82.8)	NE (7.2, NE)	2.7365 (1.8460, 4.0566) <0.0001	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Baseline CNS metastases											0.5149
Yes	24	12 (50.0)	12 (50.0)	5.5 (2.7, NE)	8	2 (25.0)	6 (75.0)	NE (1.5, NE)	1.6514 (0.3669, 7.4318) 0.5134	0.5139	
No	349	184 (52.7)	165 (47.3)	5.0 (4.2, 5.6)	176	28 (15.9)	148 (84.1)	NE (7.2, NE)	2.9194 (1.9597, 4.3490) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Renal function at baseline											0.2314
Normal Function	202	104 (51.5)	98 (48.5)	5.5 (4.1, 8.3)	87	11 (12.6)	76 (87.4)	NE (6.9, NE)	3.3877 (1.8163, 6.3185) 0.0001	<0.0001	
Mild Impairment	123	68 (55.3)	55 (44.7)	4.2 (2.9, 5.5)	69	11 (15.9)	58 (84.1)	8.3 (7.2, NE)	3.2026 (1.6919, 6.0623) 0.0004	0.0002	
Moderate Impairment	41	21 (51.2)	20 (48.8)	5.6 (4.1, NE)	23	8 (34.8)	15 (65.2)	7.2 (2.9, NE)	1.4237 (0.6297, 3.2187) 0.3960	0.3920	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.2.7.2 - Time to response based on BICR - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hepatic function at baseline											0.9674
Normal Function	170	96 (56.5)	74 (43.5)	5.4 (4.1, 6.9)	98	17 (17.3)	81 (82.7)	NE (7.2, NE)	2.8411 (1.6932, 4.7672) 0.0001	<0.0001	
Mild Impairment	195	98 (50.3)	97 (49.7)	4.6 (4.1, 5.7)	84	13 (15.5)	71 (84.5)	NE (6.9, NE)	2.7760 (1.5545, 4.9571) 0.0006	0.0003	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.2.7.2 - Time to response based on BICR - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline visceral disease										0.0351
Yes	332	173 (52.1)	159 (47.9)	5.4 (4.2, 5.7)	157	29 (18.5)	128 (81.5)	NE (7.2, NE)	2.4533 (1.6539, 3.6392) <0.0001	<0.0001
No	41	23 (56.1)	18 (43.9)	4.2 (2.8, NE)	27	1 (3.7)	26 (96.3)	NE (NE, NE)	13.7560 (1.8529, 102.1250) 0.0104	0.0008

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.2.7.2 - Time to response based on BICR - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (IXRS)										0.9048
Positive	331	176 (53.2)	155 (46.8)	5.4 (4.2, 5.6)	163	27 (16.6)	136 (83.4)	NE (7.2, NE)	2.8053 (1.8693, 4.2101) <0.0001	<0.0001
Negative	42	20 (47.6)	22 (52.4)	4.2 (2.7, NE)	21	3 (14.3)	18 (85.7)	NE (NE, NE)	3.0969 (0.9147, 10.4846) 0.0693	0.0547

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.2.7.2 - Time to response based on BICR - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.8306
Positive	333	176 (52.9)	157 (47.1)	5.4 (4.2, 5.6)	166	27 (16.3)	139 (83.7)	NE (7.2, NE)	2.8590 (1.9050, 4.2907) <0.0001	<0.0001	
Negative	40	20 (50.0)	20 (50.0)	4.2 (2.7, NE)	18	3 (16.7)	15 (83.3)	NE (2.8, NE)	2.6857 (0.7926, 9.1002) 0.1126	0.0972	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

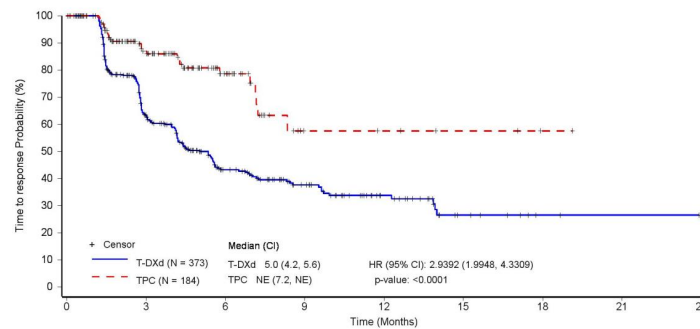
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DE.F.2.7.3 - Time to response based on BICR - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

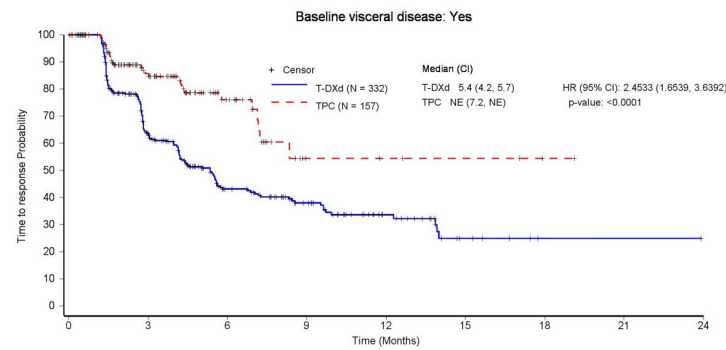
	0	3	6	9	12	15	18	21	24
T-DXd (N = 373)	373	192	89	53	27	9	2	1	0
TPC (N = 184)	184	92	33	6	5	3	1	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:10; Program name: F1\_OS\_3\_FAS.sas; Output name: F2\_TTR\_BICR\_3\_FAS.rf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24
T-DXd (N = 332)	332	170	77	48	23	7	1	1	0
TPC (N = 157)	157	79	28	5	4	3	1	0	0

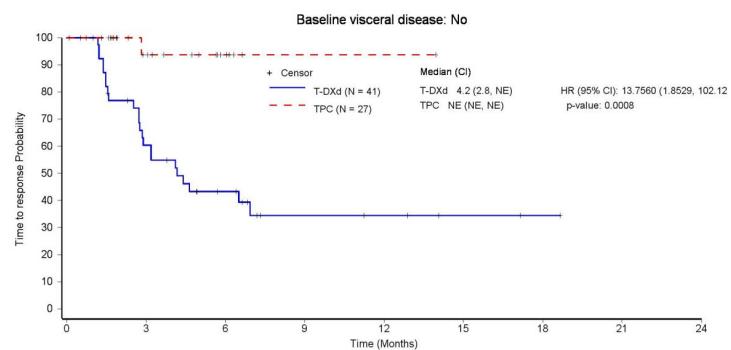
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:10; Program name: F1\_OS\_4\_FAS.sas; Output name: F2\_TTR\_BICR\_4\_FAS.rf



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Patients still at risk:

T-DXd (N = 41)	41	22	12	5	4	2	1	0	0
TPC (N = 27)	27	13	5	1	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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**Anhang 4-G 2.2.6: Dauer des Ansprechens**

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DE.T.2.4.1 - Duration of response based on BICR - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with response, n (%)	196 (52.5)	30 (16.3)	
Number of subjects with events, n (%)	113 (57.7)	20 (66.7)	
Number of subjects censored, n (%)	83 (42.3)	10 (33.3)	
Median time to first event (months) [a]	10.7	6.8	
95% Confidence Interval	[8.5, 13.2]	[6.0, 9.9]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.6397
95% Confidence Interval			[0.3861, 1.0598]
p-value			0.0828
Stratified log-rank p-value [c]			0.0805

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set, for number of subjects with events and number of subjects censored: proportion of number of subjects with response; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.2.4.2 - Duration of response based on BICR - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=196)			TPC (N=30)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.7111
HER2 IHC 1+	105	57 (54.3)	48 (45.7)	11.1 (8.3, 16.3)	18	12 (66.7)	6 (33.3)	6.9 (6.0, 9.9)	0.6710 (0.3576, 1.2591) 0.2140	0.2111
HER2 IHC 2+/ISH Negative	91	56 (61.5)	35 (38.5)	9.7 (8.0, 13.7)	12	8 (66.7)	4 (33.3)	6.6 (3.7, 15.3)	0.5679 (0.2667, 1.2094) 0.1424	0.1360

N: number of subjects with response in analysis set; Nsub: number of subjects with response in subgroup category; %: proportion of number of subjects with response in analysis set; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.2.4.2 - Duration of response based on BICR - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=196)			TPC (N=30)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.4455
1	113	60 (53.1)	53 (46.9)	11.0 (8.7, 15.3)	19	11 (57.9)	8 (42.1)	6.8 (5.6, NE)	0.7246 (0.3788, 1.3863)	0.3257
>=2	82	52 (63.4)	30 (36.6)	8.9 (7.2, 13.1)	11	9 (81.8)	2 (18.2)	6.7 (3.7, 8.7)	0.5063 (0.2441, 1.0499)	0.0629

N: number of subjects with response in analysis set; Nsub: number of subjects with response in subgroup category; %: proportion of number of subjects with response in analysis set; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=196)			TPC (N=30)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Prior CDK4/6											
Yes	119	67 (56.3)	52 (43.7)	9.5 (7.3, 12.2)	15	9 (60.0)	6 (40.0)	8.7 (4.7, NE)	0.8196 (0.4065, 1.6524)	0.5753	0.4843
No	57	33 (57.9)	24 (42.1)	13.2 (9.7, 16.8)	12	9 (75.0)	3 (25.0)	6.8 (5.6, 15.3)	0.5291 (0.2489, 1.1248)	0.0920	

N: number of subjects with response in analysis set; Nsub: number of subjects with response in subgroup category; %: proportion of number of subjects with response in analysis set; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=196)			TPC (N=30)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Age											
<65	156	89 (57.1)	67 (42.9)	10.4 (8.3, 13.7)	20	12 (60.0)	8 (40.0)	6.8 (5.1, NE)	0.8275 (0.4511, 1.5179) 0.5407	0.5397	0.1499
>=65	40	24 (60.0)	16 (40.0)	11.1 (7.4, 19.4)	10	8 (80.0)	2 (20.0)	6.6 (3.1, 7.9)	0.2891 (0.1213, 0.6889) 0.0051	0.0030	

N: number of subjects with response in analysis set; Nsub: number of subjects with response in subgroup category; %: proportion of number of subjects with response in analysis set; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=196)			TPC (N=30)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Age											
<75	189	109 (57.7)	80 (42.3)	10.8 (8.6, 13.7)	27	18 (66.7)	9 (33.3)	6.8 (5.6, 9.9)	0.6431 (0.3884, 1.0647) 0.0861	0.0828	0.7745
>=75	7	4 (57.1)	3 (42.9)	7.1 (3.2, NE)	3	2 (66.7)	1 (33.3)	6.9 (6.0, 6.9)	0.4732 (0.0659, 3.3972) 0.4569	0.4466	

N: number of subjects with response in analysis set; Nsub: number of subjects with response in subgroup category; %: proportion of number of subjects with response in analysis set; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=196)			TPC (N=30)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Race										0.0711
White	95	58 (61.1)	37 (38.9)	9.5 (7.3, 13.1)	16	9 (56.3)	7 (43.8)	8.7 (6.0, NE)	0.9670 (0.4764, 1.9632)	0.9238
Non-White	101	55 (54.5)	46 (45.5)	11.9 (8.9, 15.2)	14	11 (78.6)	3 (21.4)	6.6 (4.7, 7.9)	0.3990 (0.2054, 0.7751)	0.0050

N: number of subjects with response in analysis set; Nsub: number of subjects with response in subgroup category; %: proportion of number of subjects with response in analysis set; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=196)			TPC (N=30)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]	
Region										0.9195	
Asia	79	45 (57.0)	34 (43.0)	11.9 (8.3, 15.2)	9	6 (66.7)	3 (33.3)	6.6 (3.1, 15.3)	0.5509 (0.2320, 1.3080)	0.1680	
North America	26	19 (73.1)	7 (26.9)	9.8 (5.6, 12.2)	7	4 (57.1)	3 (42.9)	6.8 (2.8, NE)	0.8099 (0.2680, 2.4472)	0.7082	
Europe + Israel	91	49 (53.8)	42 (46.2)	9.5 (7.4, 16.8)	14	10 (71.4)	4 (28.6)	7.4 (4.9, 9.9)	0.7086 (0.3514, 1.3852)	0.2980	

N: number of subjects with response in analysis set; Nsub: number of subjects with response in subgroup category; %: proportion of number of subjects with response in analysis set; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=196)			TPC (N=30)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	110	65 (59.1)	45 (40.9)	10.7 (8.3, 15.3)	17	10 (58.8)	7 (41.2)	7.9 (5.6, NE)	0.8357 (0.4263, 1.6386) 0.6014	0.5974	0.1190
1	86	48 (55.8)	38 (44.2)	10.8 (7.6, 13.9)	13	10 (76.9)	3 (23.1)	6.5 (3.7, 6.7)	0.3911 (0.1912, 0.7998) 0.0101	0.0079	

N: number of subjects with response in analysis set; Nsub: number of subjects with response in subgroup category; %: proportion of number of subjects with response in analysis set; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=196)			TPC (N=30)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Number of lines of endocrine therapy received in the metastatic setting									0.0182	
0	29	17 (58.6)	12 (41.4)	10.4 (8.1, 13.9)	6	5 (83.3)	1 (16.7)	6.0 (3.3, 15.3)	0.4408 (0.1596, 1.2174)	0.1029
1	61	39 (63.9)	22 (36.1)	9.5 (5.9, 13.7)	10	6 (60.0)	4 (40.0)	6.9 (5.1, NE)	1.0350 (0.4329, 2.4746)	0.9404
2	59	29 (49.2)	30 (50.8)	12.2 (8.0, NE)	10	9 (90.0)	1 (10.0)	6.7 (2.8, 7.9)	0.9383 (0.3276, 0.0043)	0.0027

N: number of subjects with response in analysis set; Nsub: number of subjects with response in subgroup category; %: proportion of number of subjects with response in analysis set; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Subgroup	T-DXd (N=196)			TPC (N=30)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
>=3	47	28 (59.6)	19 (40.4)	10.8 (6.8, 19.5)	4	0	4 (100)	NE (NE, NE)	NE (NE, NE)	0.1562	0.9912

N: number of subjects with response in analysis set; Nsub: number of subjects with response in subgroup category; %: proportion of number of subjects with response in analysis set; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=196)			TPC (N=30)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.5681
PD	88	53 (60.2)	35 (39.8)	8.6 (7.0, 11.1)	14	12 (85.7)	2 (14.3)	6.1 (3.3, 6.8)	0.5254 (0.2790, 0.9894)	0.0423
PR	31	20 (64.5)	11 (35.5)	9.9 (6.7, 12.6)	3	2 (66.7)	1 (33.3)	7.9 (6.6, NE)	1.1145 (0.2592, 4.7915)	0.8861
SD	39	22 (56.4)	17 (43.6)	13.7 (7.4, 19.5)	9	5 (55.6)	4 (44.4)	8.7 (6.0, 15.3)	0.7146 (0.2632, 1.9397)	0.5033

N: number of subjects with response in analysis set; Nsub: number of subjects with response in subgroup category; %: proportion of number of subjects with response in analysis set; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Subgroup	T-DXd (N=196)			TPC (N=30)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.7737
Yes	18	14 (77.8)	4 (22.2)	8.7 (5.3, 13.9)	1	1 (100)	0	6.6 (NE, NE)	0.4222 (0.0506, 3.5207)	0.4113
No	178	99 (55.6)	79 (44.4)	11.0 (8.5, 13.7)	29	19 (65.5)	10 (34.5)	6.8 (6.0, 9.9)	0.6374 (0.3878, 1.0476)	0.0725

N: number of subjects with response in analysis set; Nsub: number of subjects with response in subgroup category; %: proportion of number of subjects with response in analysis set; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 16SEP2022 – 17:01; Program name: T1\_OS\_2\_FAS.sas; Output name: T2\_DOR\_BICR\_2\_FAS.rtf

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Subgroup	T-DXd (N=196)			TPC (N=30)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Baseline CNS metastases											
Yes	12	9 (75.0)	3 (25.0)	7.1 (3.9, 13.9)	2	2 (100)	0	4.9 (3.3, 6.6)	0.3870 (0.0743, 2.0157)	0.2422	0.5514
No	184	104 (56.5)	80 (43.5)	11.0 (8.7, 13.7)	28	18 (64.3)	10 (35.7)	6.8 (6.0, 9.9)	0.6580 (0.3965, 1.0918)	0.1023	

N: number of subjects with response in analysis set; Nsub: number of subjects with response in subgroup category; %: proportion of number of subjects with response in analysis set; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 16SEP2022 – 17:01; Program name: T1\_OS\_2\_FAS.sas; Output name: T2\_DOR\_BICR\_2\_FAS.rtf



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Subgroup	T-DXd (N=196)			TPC (N=30)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Renal function at baseline										0.3930
Normal Function	104	62 (59.6)	42 (40.4)	10.2 (8.5, 13.7)	11	7 (63.6)	4 (36.4)	8.7 (3.7, NE)	0.8467 (0.3859, 1.8577)	0.6747
Mild Impairment	68	39 (57.4)	29 (42.6)	10.8 (7.0, 16.8)	11	9 (81.8)	2 (18.2)	6.6 (3.1, 7.9)	0.4753 (0.2257, 1.0010)	0.0456
Moderate Impairment	21	10 (47.6)	11 (52.4)	11.1 (5.4, NE)	8	4 (50.0)	4 (50.0)	6.9 (5.6, 9.9)	0.0503 (0.1904, 2.2052)	0.4845

N: number of subjects with response in analysis set; Nsub: number of subjects with response in subgroup category; %: proportion of number of subjects with response in analysis set; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.2.4.2 - Duration of response based on BICR - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=196)			TPC (N=30)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Hepatic function at baseline										0.8774
Normal Function	96	48 (50.0)	48 (50.0)	11.1 (8.5, 19.3)	17 (64.7)	11 (35.3)	6 (6.0, 15.3)	0.6186 (0.3185, 1.2014) 0.1561	0.1519	
Mild Impairment	98	63 (64.3)	35 (35.7)	9.8 (7.4, 13.2)	13 (69.2)	9 (30.8)	4 (4.7, 9.9)	0.5930 (0.2896, 1.2144) 0.1530	0.1458	

N: number of subjects with response in analysis set; Nsub: number of subjects with response in subgroup category; %: proportion of number of subjects with response in analysis set; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 16SEP2022 – 17:01; Program name: T1\_OS\_2\_FAS.sas; Output name: T2\_DOR\_BICR\_2\_FAS.rtf

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DE.T.2.4.2 - Duration of response based on BICR - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=196)			TPC (N=30)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline visceral disease										NE
Yes	173	101 (58.4)	72 (41.6)	10.2 (8.1, 12.2)	29	20 (69.0)	9 (31.0)	6.8 (6.0, 9.9)	0.6849 (0.4214, 1.1129)	0.1229
No	23	12 (52.2)	11 (47.8)	15.2 (8.3, 19.4)	1	0	1 (100)	NE (NE, NE)	1.0000 (0.0000, )	1.0000

N: number of subjects with response in analysis set; Nsub: number of subjects with response in subgroup category; %: proportion of number of subjects with response in analysis set; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 16SEP2022 – 17:01; Program name: T1\_OS\_2\_FAS.sas; Output name: T2\_DOR\_BICR\_2\_FAS.rtf

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DE.T.2.4.2 - Duration of response based on BICR - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=196)			TPC (N=30)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Hormon receptor status (IXRS)											
Positive	176	100 (56.8)	76 (43.2)	10.7 (8.5, 13.7)	27	18 (66.7)	9 (33.3)	6.8 (6.5, 9.9)	0.6818 (0.4102, 1.1332)	0.1363	0.2510
Negative	20	13 (65.0)	7 (35.0)	8.6 (7.1, 13.9)	3	2 (66.7)	1 (33.3)	4.9 (3.7, 6.0)	0.1507 (0.0272, 0.8353)	0.0114	

N: number of subjects with response in analysis set; Nsub: number of subjects with response in subgroup category; %: proportion of number of subjects with response in analysis set; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 16SEP2022 – 17:01; Program name: T1\_OS\_2\_FAS.sas; Output name: T2\_DOR\_BICR\_2\_FAS.rtf

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DE.T.2.4.2 - Duration of response based on BICR - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=196)			TPC (N=30)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Hormon receptor status (derived)											
Positive	176	100 (56.8)	76 (43.2)	10.7 (8.5, 13.7)	27	18 (66.7)	9 (33.3)	6.8 (6.5, 9.9)	0.6816 (0.4101, 1.1328) 0.1392	0.1359	0.2529
Negative	20	13 (65.0)	7 (35.0)	8.6 (7.1, 13.9)	3	2 (66.7)	1 (33.3)	4.9 (3.7, 6.0)	0.1507 (0.0272, 0.8353) 0.0303	0.0114	

N: number of subjects with response in analysis set; Nsub: number of subjects with response in subgroup category; %: proportion of number of subjects with response in analysis set; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

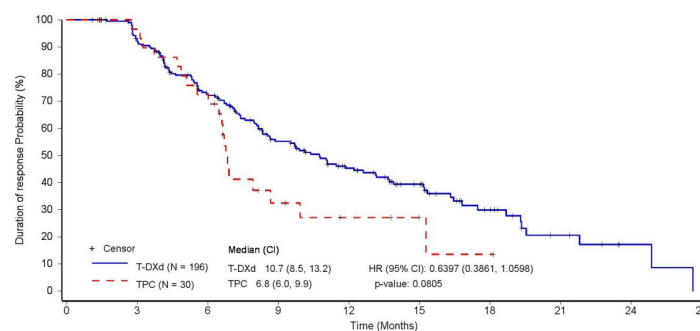
[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 16SEP2022 – 17:01; Program name: T1\_OS\_2\_FAS.sas; Output name: T2\_DOR\_BICR\_2\_FAS.rtf

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Patients still at risk:

T-DXd (N = 196)	196	173	125	83	58	38	17	7	2	0
TPC (N = 30)	30	28	21	7	4	2	1	0	0	0

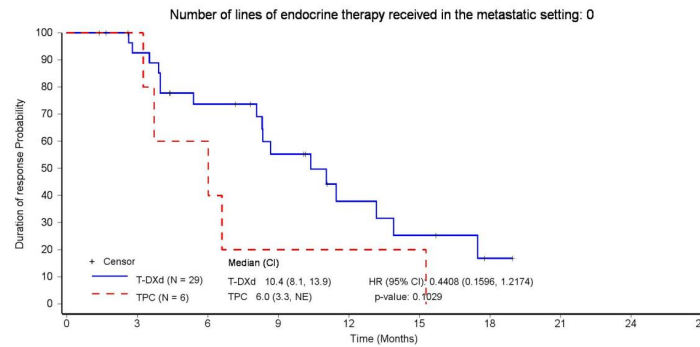
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:09; Program name: F1\_OS\_3\_FAS.sas; Output name: F2\_DOR\_BICR\_3\_FAS.rf

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DE.F.2.4.4 - Duration of response based on BICR - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27
T-DXd (N = 29)	29	25	18	12	6	4	1	0	0	0
TPC (N = 6)	6	5	3	1	1	1	0	0	0	0

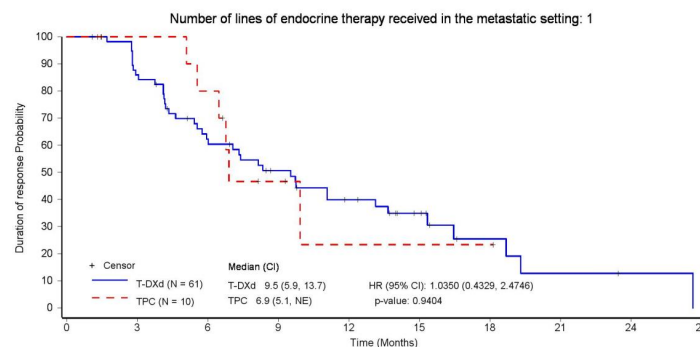
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:10; Program name: F1\_OS\_4\_FAS.sas; Output name: F2\_DOR\_BICR\_4\_FAS.rf

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DE.F.2.4.4 - Duration of response based on BICR - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27
T-DXd (N = 61)	61	49	33	24	17	10	4	2	1	0
TPC (N = 10)	10	10	8	3	1	1	1	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

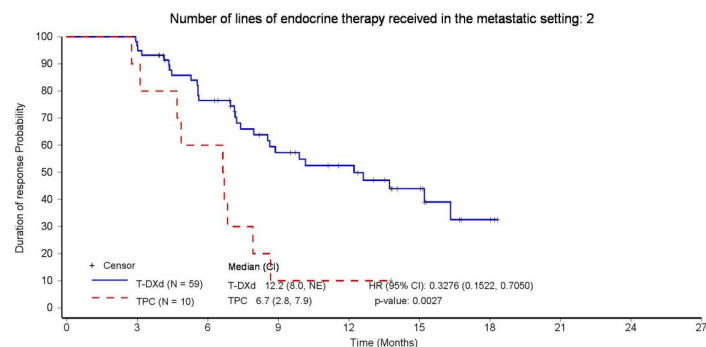
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 Run date: 21OCT2022 – 18:10; Program name: F1\_OS\_4\_FAS.sas; Output name: F2\_DOR\_BICR\_4\_FAS.rf



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DE.F.2.4.4 - Duration of response based on BICR - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27
T-DXd (N = 59)	59	57	41	26	20	11	3	0	0	0
TPC (N = 10)	10	9	6	1	1	0	0	0	0	0

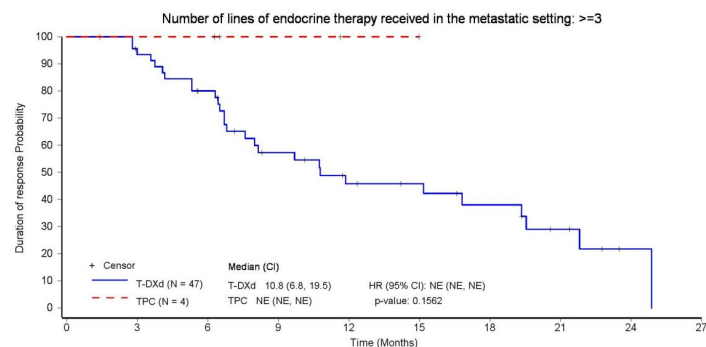
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:10; Program name: F1\_OS\_4\_FAS.sas; Output name: F2\_DOR\_BICR\_4\_FAS.rf

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DE.F.2.4.4 - Duration of response based on BICR - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

T-DXd (N = 47)	47	42	33	21	15	13	9	5	1	0
TPC (N = 4)	4	4	4	2	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:10; Program name: F1\_OS\_4\_FAS.sas; Output name: F2\_DOR\_BICR\_4\_FAS.rf

**Anhang 4-G 2.3: Zeit bis zur Hospitalisierung**

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DE.T.2.10.1 - Time to first hospitalization - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	90 (24.1)	33 (17.9)	
Number of subjects censored, n (%)	283 (75.9)	151 (82.1)	
Median time to first event (months) [a]	NE	NE	
95% Confidence Interval	[24.4, NE]	[9.3, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.7716
95% Confidence Interval			[0.5108, 1.1657]
p-value			0.2181
Stratified log-rank p-value [c]			0.2168

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 15SEP2022 – 11:57; Program name: T2\_HOSP\_1\_FAS.sas; Output name: T2\_HOSP\_1\_FAS.rtf

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DE.T.2.10.2 - Time to first hospitalization - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.1430
HER2 IHC 1+	214	51 (23.8)	163 (76.2)	NE (NE, NE)	107	14 (13.1)	93 (86.9)	NE (NE, NE)	1.0958 (0.5993, 2.0038) 0.7664	0.7670
HER2 IHC 2+/ISH Negative	159	39 (24.5)	120 (75.5)	24.4 (24.4, NE)	77	19 (24.7)	58 (75.3)	NE (7.1, NE)	0.5430 (0.3087, 0.9550) 0.0340	0.0317

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting									0.8436
1	221 (19.9)	177 (80.1)	NE (24.4, NE)	100 (16.0)	84 (84.0)	NE (9.3, NE)	0.7390 (0.4111, 1.3284)	0.3106	
>=2	151 (30.5)	105 (69.5)	NE (11.9, NE)	83 (20.5)	66 (79.5)	NE (6.2, NE)	0.8155 (0.4601, 1.4455)	0.4825	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Prior CDK4/6											
Yes	235	52 (22.1)	183 (77.9)	24.4 (24.4, NE)	118	21 (17.8)	97 (82.2)	NE (9.3, NE)	0.6971 (0.4119, 1.1797) 0.1789	0.1766	0.5515
No	98	27 (27.6)	71 (72.4)	NE (NE, NE)	48	9 (18.8)	39 (81.3)	NE (8.6, NE)	0.9086 (0.4246, 1.9441) 0.8049	0.8060	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.2.10.2 - Time to first hospitalization - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Age											
<65	290	65 (22.4)	225 (77.6)	NE (24.4, NE)	136	24 (17.6)	112 (82.4)	NE (NE, NE)	0.7294 (0.4509, 1.1802) 0.1987	0.1969	0.3217
>=65	83	25 (30.1)	58 (69.9)	NE (9.0, NE)	48	9 (18.8)	39 (81.3)	NE (6.2, NE)	0.9340 (0.4302, 2.0280) 0.8630	0.8624	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Age											
<75	359	88 (24.5)	271 (75.5)	NE (24.4, NE)	175	30 (17.1)	145 (82.9)	NE (9.3, NE)	0.8105 (0.5295, 1.2405) 0.3333	0.3321	0.3387
>=75	14	2 (14.3)	12 (85.7)	NE (5.5, NE)	9	3 (33.3)	6 (66.7)	NE (0.6, NE)	0.2805 (0.0460, 1.7099) 0.1681	0.1424	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Race										0.4588
White	176	42 (23.9)	134 (76.1)	24.4 (24.4, NE)	91	18 (19.8)	73 (80.2)	NE (9.3, NE)	0.7278 (0.4130, 1.2825) 0.2717	0.2705
Non-White	197	48 (24.4)	149 (75.6)	NE (NE, NE)	92	15 (16.3)	77 (83.7)	NE (8.6, NE)	0.8211 (0.4537, 1.4862) 0.5150	0.5144

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Region										0.3626
Asia	147	37 (25.2)	110 (74.8)	NE (NE, NE)	66	9 (13.6)	57 (86.4)	NE (NE, NE)	0.9097 (0.4317, 1.9168) 0.8035	0.8031
North America	60	20 (33.3)	40 (66.7)	11.9 (7.8, NE)	33	6 (18.2)	27 (81.8)	9.3 (4.5, NE)	0.9350 (0.3649, 2.3955) 0.8886	0.8866
Europe + Israel	166	33 (19.9)	133 (80.1)	24.4 (24.4, NE)	85	18 (21.2)	67 (78.8)	NE (8.6, NE)	0.6340 (0.3519, 1.1420) 0.1291	0.1255

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	200	34 (17.0)	166 (83.0)	NE (24.4, NE)	105	16 (15.2)	89 (84.8)	NE (NE, NE)	0.5499 (0.2982, 1.0144) 0.0556	0.0522	0.1678
1	173	56 (32.4)	117 (67.6)	13.1 (11.6, NE)	79	17 (21.5)	62 (78.5)	NE (9.3, NE)	0.9780 (0.5599, 1.7081) 0.9377	0.9364	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting										0.7144
0	60	16 (26.7)	44 (73.3)	NE (8.8, NE)	34	6 (17.6)	28 (82.4)	NE (4.8, NE)	0.8137 (0.3111, 2.1283)	0.6720
1	108	21 (19.4)	87 (80.6)	NE (NE, NE)	51	6 (11.8)	45 (88.2)	NE (NE, NE)	1.0204 (0.4080, 2.5521)	0.9667
2	115	33 (28.7)	82 (71.3)	NE (11.9, NE)	54	14 (25.9)	40 (74.1)	NE (5.2, NE)	0.6701 (0.3518, 1.2763)	0.2200
>=3	90	20 (22.2)	70 (77.8)	NE (24.4, NE)	45	7 (15.6)	38 (84.4)	9.3 (7.1, NE)	0.6716 (0.2707, 1.6662)	0.3872

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.9605
PD	174	36 (20.7)	138 (79.3)	24.4 (24.4, NE)	85	13 (15.3)	72 (84.7)	NE (8.6, NE)	0.7255 (0.3776, 1.3939)	0.3333
PR	48	12 (25.0)	36 (75.0)	NE (11.6, NE)	22	4 (18.2)	18 (81.8)	NE (6.2, NE)	0.7599 (0.2327, 2.4823)	0.6486
SD	82	21 (25.6)	61 (74.4)	NE (NE, NE)	55	10 (18.2)	45 (81.8)	NE (7.1, NE)	0.9141 (0.4223, 1.9789)	0.8178

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.1754
Yes	37	11 (29.7)	26 (70.3)	24.4 (9.0, 24.4)	15	5 (33.3)	10 (66.7)	NE (0.8, NE)	0.3045 (0.0955, 0.9703) 0.0443	0.0333
No	336	79 (23.5)	257 (76.5)	NE (NE, NE)	169	28 (16.6)	141 (83.4)	NE (NE, NE)	0.8475 (0.5455, 1.3165) 0.4614	0.4597

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.8090
Yes	24	8 (33.3)	16 (66.7)	24.4 (9.0, 24.4)	8	2 (25.0)	6 (75.0)	NE (0.2, NE)	0.4455 (0.0833, 2.3842) 0.3448	0.3256
No	349	82 (23.5)	267 (76.5)	NE (NE, NE)	176	31 (17.6)	145 (82.4)	NE (9.3, NE)	0.7909 (0.5183, 1.2069) 0.2766	0.2751

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Renal function at baseline											0.7137
Normal Function	202	46 (22.8)	156 (77.2)	24.4 (24.4, NE)	87	16 (18.4)	71 (81.6)	NE (9.3, NE)	0.6350 (0.3518, 1.1464) 0.1319	0.1283	
Mild Impairment	123	32 (26.0)	91 (74.0)	NE (NE, NE)	69	11 (15.9)	58 (84.1)	NE (6.2, NE)	0.9043 (0.4488, 1.8221) 0.7784	0.7783	
Moderate Impairment	41	12 (29.3)	29 (70.7)	NE (11.9, NE)	23	6 (26.1)	17 (73.9)	NE (8.6, NE)	0.9995 (0.3742, 2.6694) 0.9992	0.9992	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.0319
Normal Function	170	49 (28.8)	121 (71.2)	NE (NE, NE)	98	14 (14.3)	84 (85.7)	NE (NE, NE)	1.1418 (0.6230, 2.0925) 0.6679	0.6687
Mild Impairment	195	39 (20.0)	156 (80.0)	24.4 (24.4, NE)	84	19 (22.6)	65 (77.4)	NE (9.3, NE)	0.4920 (0.2785, 0.8690) 0.0145	0.0129

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.2.10.2 - Time to first hospitalization - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline visceral disease										0.1098
Yes	332	81 (24.4)	251 (75.6)	NE (24.4, NE)	157	32 (20.4)	125 (79.6)	NE (9.3, NE)	0.7066 (0.4647, 1.0744) 0.1043	0.1027
No	41	9 (22.0)	32 (78.0)	NE (NE, NE)	27	1 (3.7)	26 (96.3)	NE (NE, NE)	2.3574 (0.2827, 19.6586) 0.4281	0.4152

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (IXRS)										0.5824
Positive	331	79 (23.9)	252 (76.1)	NE (24.4, NE)	163	28 (17.2)	135 (82.8)	NE (NE, NE)	0.8017 (0.5157, 1.2463) 0.3262	0.3253
Negative	42	11 (26.2)	31 (73.8)	NE (8.8, NE)	21	5 (23.8)	16 (76.2)	NE (3.7, NE)	0.5643 (0.1810, 1.7591) 0.3239	0.3184

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.2.10.2 - Time to first hospitalization - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (derived)										0.7693
Positive	333	78 (23.4)	255 (76.6)	NE (24.4, NE)	166	30 (18.1)	136 (81.9)	NE (NE, NE)	0.7554 (0.4908, 1.1626) 0.2023	0.2009
Negative	40	12 (30.0)	28 (70.0)	NE (8.8, NE)	18	3 (16.7)	15 (83.3)	NE (4.8, NE)	0.8262 (0.2133, 3.1992) 0.7822	0.7819

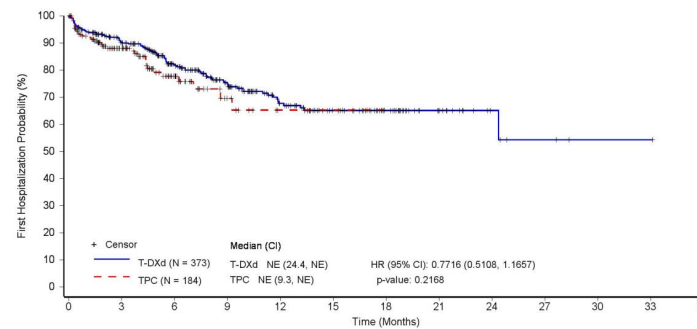
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.2.10.3 - Time to first hospitalization - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

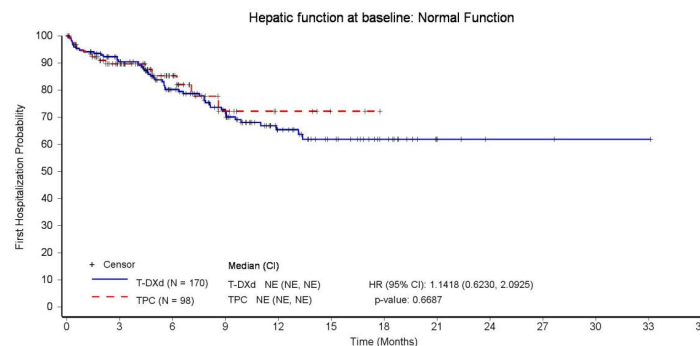
	0	3	6	9	12	15	18	21	24	27	30	33	36
T-DXd (N = 373)	373	295	210	148	86	56	36	18	6	3	1	1	0
TPC (N = 184)	184	104	43	17	8	5	0	0	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:11; Program name: F2\_HOSP\_3\_FAS.sas; Output name: F2\_HOSP\_3\_FAS.rf

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Patients still at risk:

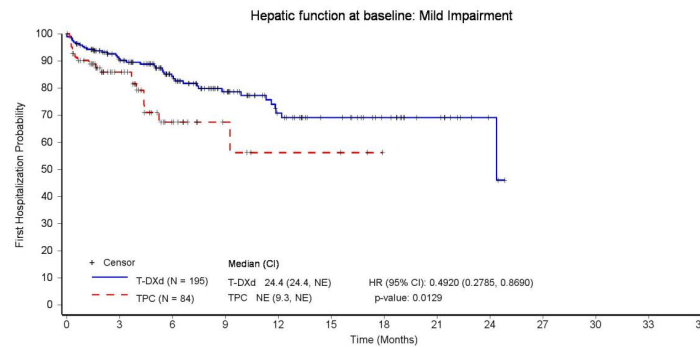
	0	3	6	9	12	15	18	21	24	27	30	33	36
T-DXd (N = 170)	170	144	107	81	43	26	15	5	2	2	1	1	0
TPC (N = 98)	98	60	29	11	5	2	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:11; Program name: F2\_HOSP\_4\_FAS.sas; Output name: F2\_HOSP\_4\_FAS.rf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33	36
T-DXd (N = 195)	195	148	101	65	42	29	20	12	3	0	0	0	0
TPC (N = 84)	84	44	14	6	3	3	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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**Anhang 4-G 3: Ergänzende Analysen DESTINY-Breast04: Patientenberichtete Fragebögen**

**Anhang 4-G 3.1: EQ-5D-5L VAS**

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DE.T.3.1.1 - EQ-5D-5L VAS - First deterioration - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

EQ-5D-5L VAS

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	144 (38.6)	60 (32.6)	
Number of subjects censored, n (%)	229 (61.4)	124 (67.4)	
Median time to first event (months) [a]	16.4	8.4	
95% Confidence Interval	[11.1, NE]	[6.1, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.8075
95% Confidence Interval			[0.5939, 1.0978]
p-value			0.1724
Stratified log-rank p-value [c]			0.1692

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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EQ-5D-5L VAS

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
HER2 status											0.4832
HER2 IHC 1+	214	86 (40.2)	128 (59.8)	12.7 (9.9, NE)	107	32 (29.9)	75 (70.1)	NE (5.4, NE)	0.8768 (0.5810, 1.3233)	0.5399	
HER2 IHC 2+/ISH Negative	159	58 (36.5)	101 (63.5)	NE (10.3, NE)	77	28 (36.4)	49 (63.6)	7.5 (4.8, NE)	0.7339 (0.4649, 1.1584)	0.1791	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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EQ-5D-5L VAS

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.2564
1	221	94 (42.5)	127 (57.5)	13.1 (8.3, 18.3)	100	35 (35.0)	65 (65.0)	NE (4.8, NE)	0.9341 (0.6317, 1.3815) 0.7329	0.7319
>=2	151	49 (32.5)	102 (67.5)	NE (11.2, NE)	83	25 (30.1)	58 (69.9)	7.1 (5.3, NE)	0.6192 (0.3774, 1.0160) 0.0578	0.0558

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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EQ-5D-5L VAS

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Prior CDK4/6											
Yes	235	86 (36.6)	149 (63.4)	16.4 (11.1, NE)	118	36 (30.5)	82 (69.5)	8.4 (5.7, NE)	0.8148 (0.5486, 1.2101)	0.3059	0.9950
No	98	44 (44.9)	54 (55.1)	13.1 (7.9, NE)	48	19 (39.6)	29 (60.4)	7.5 (4.4, NE)	0.8320 (0.4845, 1.4285)	0.5091	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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EQ-5D-5L VAS

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Age										0.1829
<65	290	104 (35.9)	186 (64.1)	18.3 (12.7, NE)	136	43 (31.6)	93 (68.4)	7.9 (5.4, NE)	0.7424 (0.5174, 1.0653)	0.1052
>=65	83	40 (48.2)	43 (51.8)	7.2 (4.4, 13.2)	48	17 (35.4)	31 (64.6)	NE (4.7, NE)	1.1661 (0.6588, 2.0640)	0.5977

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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EQ-5D-5L VAS

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											0.3614
<75	359	137 (38.2)	222 (61.8)	16.4 (11.1, NE)	175	57 (32.6)	118 (67.4)	8.4 (5.7, NE)	0.7907 (0.5780, 1.0815) 0.1416	0.1407	
>=75	14	7 (50.0)	7 (50.0)	5.6 (3.0, NE)	9	3 (33.3)	6 (66.7)	NE (0.7, NE)	1.5001 (0.3870, 5.8145) 0.5574	0.5689	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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EQ-5D-5L VAS

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Race										0.9426
White	176	61 (34.7)	115 (65.3)	18.3 (12.6, NE)	91	26 (28.6)	65 (71.4)	8.4 (5.7, NE)	0.8229 (0.5154, 1.3139)	0.4106
Non-White	197	83 (42.1)	114 (57.9)	11.5 (9.0, NE)	92	33 (35.9)	59 (64.1)	7.5 (4.7, NE)	0.8233 (0.5481, 1.2367)	0.3502

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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EQ-5D-5L VAS

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Region											0.4360
Asia	147	69 (46.9)	78 (53.1)	11.2 (7.6, NE)	66	28 (42.4)	38 (57.6)	6.1 (4.4, NE)	0.7714 (0.4957, 1.2006) 0.2502	0.2520	
North America	60	17 (28.3)	43 (71.7)	NE (7.2, NE)	33	4 (12.1)	29 (87.9)	NE (NE, NE)	1.6394 (0.5417, 4.9614) 0.3816	0.3718	
Europe + Israel	166	58 (34.9)	108 (65.1)	18.3 (11.5, NE)	85	28 (32.9)	57 (67.1)	7.9 (5.3, NE)	0.7284 (0.4602, 1.1531) 0.1764	0.1734	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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EQ-5D-5L VAS

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.9393
0	200	83 (41.5)	117 (58.5)	13.2 (10.3, NE)	105	35 (33.3)	70 (66.7)	7.9 (5.3, NE)	0.8311 (0.5574, 1.2392)	0.3668	
1	173	61 (35.3)	112 (64.7)	18.3 (10.4, NE)	79	25 (31.6)	54 (68.4)	8.4 (4.8, NE)	0.7906 (0.4926, 1.2687)	0.3234	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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EQ-5D-5L VAS

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.8454
0	60	26 (43.3)	34 (56.7)	9.2 (4.2, NE)	34	12 (35.3)	22 (64.7)	5.3 (3.4, NE)	0.7605 (0.3800, 1.5221) 0.4393	0.4434	
1	108	39 (36.1)	69 (63.9)	16.9 (9.3, NE)	51	19 (37.3)	32 (62.7)	7.1 (4.7, NE)	0.7827 (0.4513, 1.3575) 0.3831	0.3824	
2	115	38 (33.0)	77 (67.0)	NE (12.6, NE)	54	16 (29.6)	38 (70.4)	8.4 (4.2, NE)	0.7223 (0.3952, 1.3201) 0.2904	0.2810	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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EQ-5D-5L VAS

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	41 (45.6)	49 (54.4)	11.1 (7.2, NE)	45	13 (28.9)	32 (71.1)	NE (3.0, NE)	1.0311 (0.5481, 1.9398) 0.9243	0.9223	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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EQ-5D-5L VAS

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.3836
PD	174	57 (32.8)	117 (67.2)	NE (11.1, NE)	85	26 (30.6)	59 (69.4)	7.5 (4.7, NE)	0.6826 (0.4257, 1.0947) 0.1131	0.1115	
PR	48	26 (54.2)	22 (45.8)	11.2 (5.6, 16.9)	22	5 (22.7)	17 (77.3)	NE (2.9, NE)	1.4091 (0.5292, 3.7520) 0.4925	0.4896	
SD	82	34 (41.5)	48 (58.5)	18.3 (6.7, NE)	55	22 (40.0)	33 (60.0)	7.9 (4.8, NE)	0.8036 (0.4681, 1.3795) 0.4277	0.4239	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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EQ-5D-5L VAS

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.0350
Yes	37	15 (40.5)	22 (59.5)	11.1 (6.7, NE)	15	1 (6.7)	14 (93.3)	NE (1.5, NE)	4.3436 (0.5682, 33.2022) 0.1570	0.1228	
No	336	129 (38.4)	207 (61.6)	16.4 (11.1, NE)	169	59 (34.9)	110 (65.1)	7.5 (5.4, NE)	0.7532 (0.5513, 1.0289) 0.0749	0.0740	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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EQ-5D-5L VAS

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Baseline CNS metastases											
Yes	24	11 (45.8)	13 (54.2)	10.6 (1.5, NE)	8	0	8 (100)	NE (NE, NE)	0.9936	0.0687	0.0076
No	349	133 (38.1)	216 (61.9)	16.4 (11.1, NE)	176	60 (34.1)	116 (65.9)	7.5 (5.4, NE)	0.7509 (0.5514, 1.0226)	0.0681	0.0690

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 15SEP2022 – 11:58; Program name: T3\_EQ5D\_FD\_2\_FAS.sas; Output name: T3\_EQ5D\_FD\_2\_FAS.rtf

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DE.T.3.1.2 - EQ-5D-5L VAS - First deterioration - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

EQ-5D-5L VAS

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0027
Normal Function	202	76 (37.6)	126 (62.4)	16.9 (10.4, NE)	87	28 (32.2)	59 (67.8)	7.1 (4.2, NE)	0.7700 (0.4958, 1.1960) 0.2448	0.2406	
Mild Impairment	123	48 (39.0)	75 (61.0)	13.2 (7.2, NE)	69	27 (39.1)	42 (60.9)	7.5 (4.4, NE)	0.5951 (0.3673, 0.9643) 0.0351	0.0342	
Moderate Impairment	41	18 (43.9)	23 (56.1)	11.5 (4.2, NE)	23	2 (8.7)	21 (91.3)	NE (NE, NE)	5.3099 (1.2293, 22.9363) 0.0253	0.0124	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 15SEP2022 – 11:58; Program name: T3\_EQ5D\_FD\_2\_FAS.sas; Output name: T3\_EQ5D\_FD\_2\_FAS.rtf



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DE.T.3.1.2 - EQ-5D-5L VAS - First deterioration - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

EQ-5D-5L VAS

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.5878
Normal Function	170	78 (45.9)	92 (54.1)	12.6 (9.0, 18.3)	98	35 (35.7)	63 (64.3)	8.4 (5.4, NE)	0.8806 (0.5886, 1.3172)	0.5346
Mild Impairment	195	65 (33.3)	130 (66.7)	NE (11.5, NE)	84	24 (28.6)	60 (71.4)	NE (4.8, NE)	0.7930 (0.4927, 1.2762)	0.3387

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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EQ-5D-5L VAS

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Baseline visceral disease											0.2253
Yes	332	128 (38.6)	204 (61.4)	13.4 (11.1, NE)	157	49 (31.2)	108 (68.8)	NE (6.5, NE)	0.8753 (0.6277, 1.2205) 0.4322	0.4298	
No	41	16 (39.0)	25 (61.0)	NE (6.5, NE)	27	11 (40.7)	16 (59.3)	5.3 (1.6, NE)	0.5399 (0.2408, 1.2105) 0.1346	0.1316	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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EQ-5D-5L VAS

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (IXRS)										0.9134
Positive	331	128 (38.7)	203 (61.3)	16.4 (11.1, NE)	163	54 (33.1)	109 (66.9)	8.4 (6.1, NE)	0.8072 (0.5852, 1.1135)	0.1904
Negative	42	16 (38.1)	26 (61.9)	NE (4.5, NE)	21	6 (28.6)	15 (71.4)	NE (3.4, NE)	0.9231 (0.3563, 2.3918)	0.8628

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.3.1.2 - EQ-5D-5L VAS - First deterioration - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

EQ-5D-5L VAS

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (derived)										0.9430
Positive	333	129 (38.7)	204 (61.3)	16.4 (11.1, NE)	166	55 (33.1)	111 (66.9)	8.4 (6.1, NE)	0.8169 (0.5935, 1.1243)	0.2126
Negative	40	15 (37.5)	25 (62.5)	NE (4.5, NE)	18	5 (27.8)	13 (72.2)	NE (3.4, NE)	0.8361 (0.3003, 2.3279)	0.7236

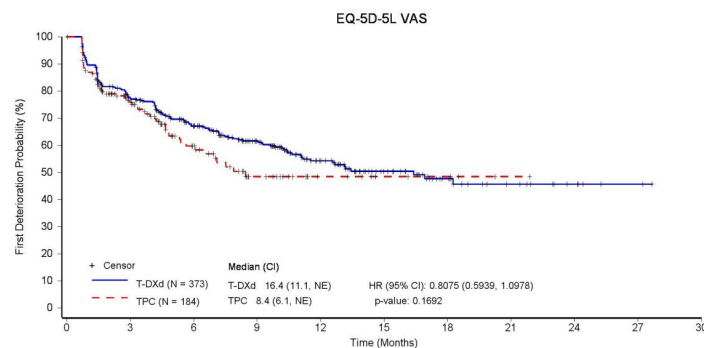
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.F.3.1.3 - EQ-5D-5L VAS - First deterioration - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

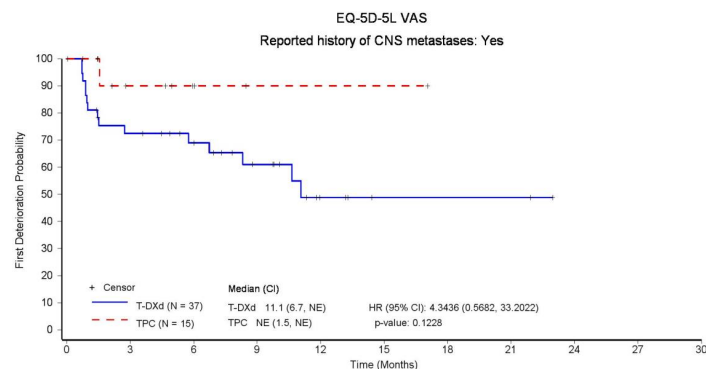
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T-DXd (N = 373)	373	251	185	136	83	47	26	14	6	2	0
TPC (N = 184)	184	94	44	21	10	6	4	1	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

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 DE.F.3.1.4 - EQ-5D-5L VAS - First deterioration - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

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Patients still at risk:

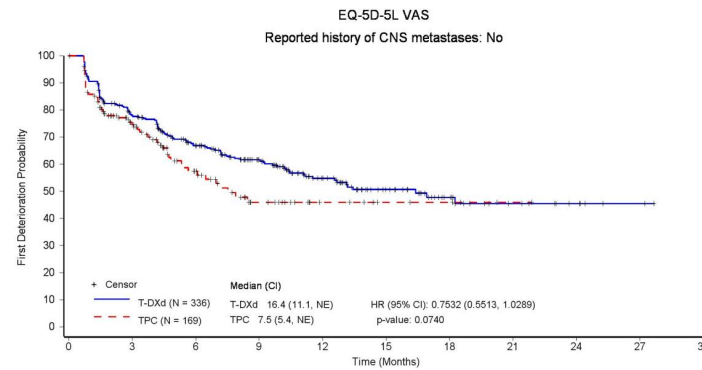
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T-DXd (N = 37)	37	25	20	13	5	2	2	2	0	0	0
TPC (N = 15)	15	7	3	1	1	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

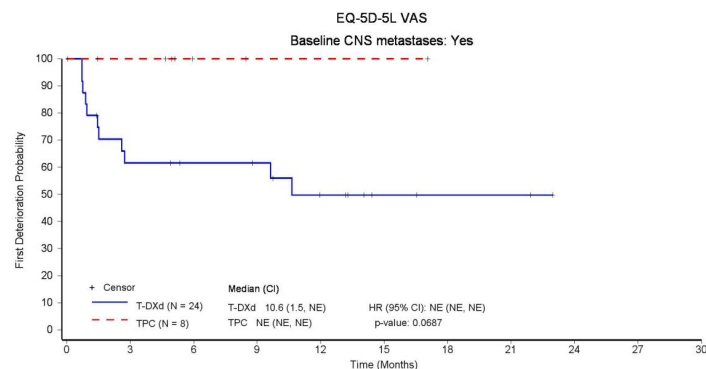
	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 336)	336	226	165	123	78	45	24	12	6	2	0
TPC (N = 169)	169	87	41	20	9	5	4	1	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 24)	24	14	12	11	7	3	2	2	0	0	0
TPC (N = 8)	8	6	2	1	1	1	0	0	0	0	0

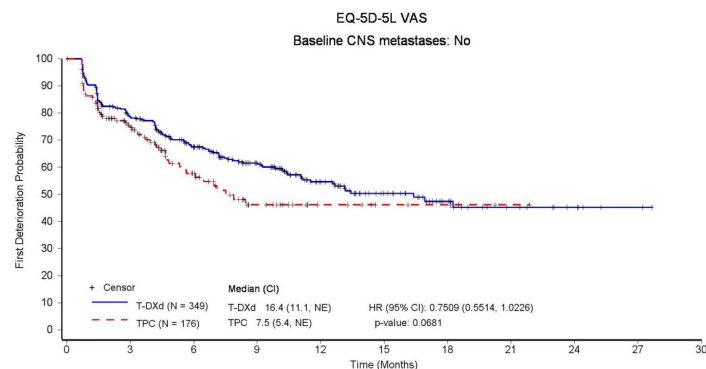
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

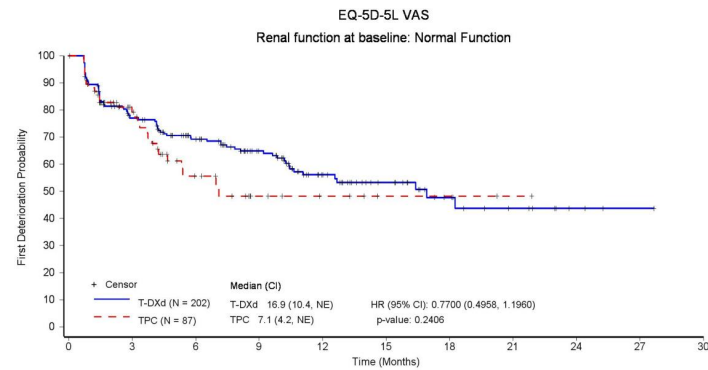
	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 349)	349	237	173	125	76	44	24	12	6	2	0
TPC (N = 176)	176	88	42	20	9	5	4	1	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

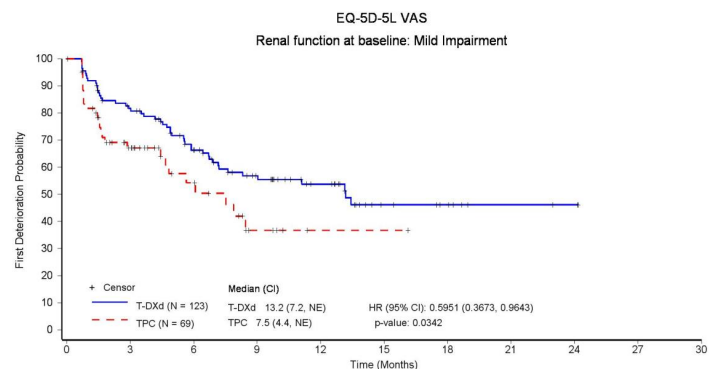
T-DXd (N = 202)	202	137	103	75	42	26	14	8	3	1	0
TPC (N = 87)	87	43	17	8	5	2	2	1	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

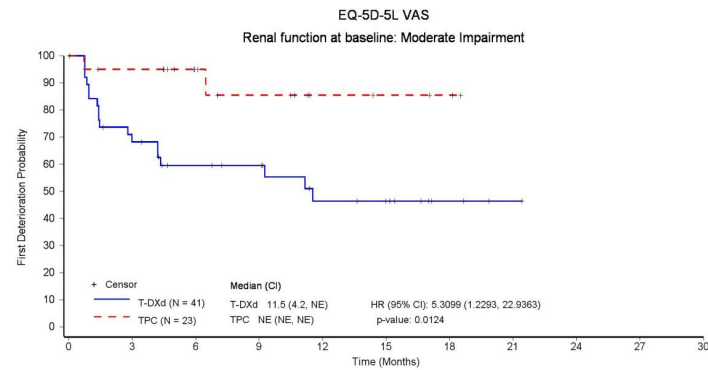
	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 123)	123	85	61	42	29	12	8	4	2	0	0
TPC (N = 69)	69	31	16	5	1	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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T-DXd (N = 41)	41	25	18	16	10	8	3	1	0	0	0
TPC (N = 23)	23	18	11	8	4	3	2	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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EQ-5D-5L VAS

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	104 (27.9)	47 (25.5)	
Number of subjects censored, n (%)	269 (72.1)	137 (74.5)	
Median time to first event (months) [a]	21.7	17.3	
95% Confidence Interval	[18.1, NE]	[8.4, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.6098
95% Confidence Interval			[0.4267, 0.8713]
p-value			0.0066
Stratified log-rank p-value [c]			0.0058

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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EQ-5D-5L VAS

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.2549
HER2 IHC 1+	214	66 (30.8)	148 (69.2)	21.7 (13.2, NE)	107	25 (23.4)	82 (76.6)	NE (8.4, NE)	0.7692 (0.4800, 1.2329)	0.2746
HER2 IHC 2+/ISH Negative	159	38 (23.9)	121 (76.1)	NE (18.1, NE)	77	22 (28.6)	55 (71.4)	17.3 (6.1, NE)	0.4802 (0.2811, 0.8201)	0.0061

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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EQ-5D-5L VAS

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.2540
1	221	69 (31.2)	152 (68.8)	21.5 (15.7, NE)	100	27 (27.0)	73 (73.0)	17.3 (8.4, NE)	0.7459 (0.4742, 1.1733) 0.2046	0.2023
>=2	151	34 (22.5)	117 (77.5)	NE (18.4, NE)	83	20 (24.1)	63 (75.9)	9.8 (6.1, NE)	0.4622 (0.2613, 0.8176) 0.0080	0.0066

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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EQ-5D-5L VAS

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Prior CDK4/6											
Yes	235	62 (26.4)	173 (73.6)	21.5 (18.1, NE)	118	28 (23.7)	90 (76.3)	17.3 (8.4, NE)	0.6283 (0.3978, 0.9922)	0.0440	0.9930
No	98	33 (33.7)	65 (66.3)	21.7 (15.7, NE)	48	16 (33.3)	32 (66.7)	NE (6.5, NE)	0.6322 (0.3438, 1.1625)	0.1367	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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EQ-5D-5L VAS

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Age											
<65	290	75 (25.9)	215 (74.1)	21.7 (18.3, NE)	136	34 (25.0)	102 (75.0)	17.3 (7.1, NE)	0.5631 (0.3716, 0.8531)	0.0067	0.2690
>=65	83	29 (34.9)	54 (65.1)	17.8 (10.2, NE)	48	13 (27.1)	35 (72.9)	NE (6.5, NE)	0.9349 (0.4809, 1.8177)	0.8427	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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EQ-5D-5L VAS

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											
<75	359	99 (27.6)	260 (72.4)	21.7 (18.3, NE)	175	45 (25.7)	130 (74.3)	17.3 (8.4, NE)	0.6082 (0.4240, 0.8725) 0.0069	0.0064	0.3241
>=75	14	5 (35.7)	9 (64.3)	17.8 (4.2, 17.8)	9	2 (22.2)	7 (77.8)	NE (3.7, NE)	1.1304 (0.2050, 6.2339) 0.8881	0.9017	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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EQ-5D-5L VAS

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Race										0.5341
White	176	39 (22.2)	137 (77.8)	NE (18.1, NE)	91	19 (20.9)	72 (79.1)	17.3 (8.4, NE)	0.5293 (0.2997, 0.9346)	0.0258
Non-White	197	65 (33.0)	132 (67.0)	21.7 (13.4, NE)	92	27 (29.3)	65 (70.7)	NE (6.5, NE)	0.7316 (0.4640, 1.1535)	0.1764

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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EQ-5D-5L VAS

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Region											0.4710
Asia	147	56 (38.1)	91 (61.9)	18.4 (12.6, NE)	66	23 (34.8)	43 (65.2)	9.8 (5.8, NE)	0.7064 (0.4318, 1.1558) 0.1665	0.1650	
North America	60	12 (20.0)	48 (80.0)	21.5 (13.2, NE)	33	3 (9.1)	30 (90.9)	NE (NE, NE)	1.1675 (0.3138, 4.3430) 0.8173	0.8157	
Europe + Israel	166	36 (21.7)	130 (78.3)	NE (18.3, NE)	85	21 (24.7)	64 (75.3)	17.3 (7.1, NE)	0.4817 (0.2773, 0.8368) 0.0095	0.0082	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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EQ-5D-5L VAS

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	200	65 (32.5)	135 (67.5)	18.4 (13.4, NE)	105	29 (27.6)	76 (72.4)	17.3 (5.8, NE)	0.6648 (0.4260, 1.0376) 0.0723	0.0705	0.7547
1	173	39 (22.5)	134 (77.5)	NE (18.3, NE)	79	18 (22.8)	61 (77.2)	NE (8.4, NE)	0.5984 (0.3361, 1.0654) 0.0810	0.0768	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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EQ-5D-5L VAS

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.9241
0	60	18 (30.0)	42 (70.0)	17.8 (10.4, NE)	34	9 (26.5)	25 (73.5)	9.8 (5.3, NE)	0.6462 (0.2854, 1.4632) 0.2950	0.2904
1	108	26 (24.1)	82 (75.9)	NE (18.1, NE)	51	16 (31.4)	35 (68.6)	17.3 (5.7, NE)	0.5620 (0.3001, 1.0525) 0.0718	0.0677
2	115	29 (25.2)	86 (74.8)	21.7 (21.5, NE)	54	11 (20.4)	43 (79.6)	NE (7.5, NE)	0.5740 (0.2768, 1.1901) 0.1356	0.1310

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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EQ-5D-5L VAS

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	31 (34.4)	59 (65.6)	18.3 (13.4, NE)	45	11 (24.4)	34 (75.6)	NE (6.5, NE)	0.7490 (0.3679, 1.5251) 0.4257	0.4254

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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EQ-5D-5L VAS

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.4116
PD	174	37 (21.3)	137 (78.7)	NE (NE, NE)	85	19 (22.4)	66 (77.6)	NE (7.1, NE)	0.5425 (0.3071, 0.9584) 0.0352	0.0325	
PR	48	22 (45.8)	26 (54.2)	16.0 (11.2, 21.5)	22	4 (18.2)	18 (81.8)	NE (5.8, NE)	0.9934 (0.3267, 3.0203) 0.9907	0.9884	
SD	82	26 (31.7)	56 (68.3)	21.7 (18.3, NE)	55	17 (30.9)	38 (69.1)	9.8 (6.5, NE)	0.6554 (0.3516, 1.2216) 0.1835	0.1799	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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EQ-5D-5L VAS

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										
Yes	37	11 (29.7)	26 (70.3)	18.1 (10.6, NE)	15	0	15 (100)	NE (NE, NE)	0.9943	0.1131
No	336	93 (27.7)	243 (72.3)	21.7 (18.3, NE)	169	47 (27.8)	122 (72.2)	17.3 (7.5, NE)	0.5774 (0.4033, 0.8266)	0.0024

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.3.2.2 - EQ-5D-5L VAS - Definitive deterioration - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

EQ-5D-5L VAS

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Baseline CNS metastases											0.0234
Yes	24	8 (33.3)	16 (66.7)	NE (5.9, NE)	8	0	8 (100)	NE (NE, NE)	NE (NE, NE) 0.9949	0.1586	
No	349	96 (27.5)	253 (72.5)	21.7 (18.1, NE)	176	47 (26.7)	129 (73.3)	17.3 (7.5, NE)	0.5830 (0.4079, 0.8334) 0.0031	0.0027	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 15SEP2022 – 11:59; Program name: T3\_EQ5D\_FD\_2\_FAS.sas; Output name: T3\_EQ5D\_DD\_2\_FAS.rtf

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EQ-5D-5L VAS

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Renal function at baseline										0.0074
Normal Function	202	53 (26.2)	149 (73.8)	21.7 (18.1, NE)	87	22 (25.3)	65 (74.7)	NE (7.1, NE)	0.5546 (0.3324, 0.9255) 0.0240	0.0219
Mild Impairment	123	38 (30.9)	85 (69.1)	18.4 (13.2, NE)	69	21 (30.4)	48 (69.6)	8.4 (5.8, 17.3)	0.4943 (0.2832, 0.8629) 0.0132	0.0116
Moderate Impairment	41	12 (29.3)	29 (70.7)	NE (11.1, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	6.5897 (0.8549, 50.7936) 0.0704	0.0369

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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EQ-5D-5L VAS

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.7633
Normal Function	170	55 (32.4)	115 (67.6)	18.3 (16.0, NE)	98	27 (27.6)	71 (72.4)	NE (8.4, NE)	0.6559 (0.4092, 1.0512) 0.0797	0.0770
Mild Impairment	195	48 (24.6)	147 (75.4)	NE (18.4, NE)	84	19 (22.6)	65 (77.4)	17.3 (6.5, NE)	0.6137 (0.3561, 1.0575) 0.0786	0.0754

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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EQ-5D-5L VAS

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline visceral disease										0.7467
Yes	332	91 (27.4)	241 (72.6)	21.7 (18.1, NE)	157	39 (24.8)	118 (75.2)	17.3 (8.8, NE)	0.6512 (0.4444, 0.9543) 0.0278	0.0268
No	41	13 (31.7)	28 (68.3)	NE (11.6, NE)	27	8 (29.6)	19 (70.4)	5.8 (4.7, NE)	0.5446 (0.2147, 1.3813) 0.2006	0.1952

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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EQ-5D-5L VAS

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (IXRS)										0.6604
Positive	331	95 (28.7)	236 (71.3)	21.7 (18.1, NE)	163	44 (27.0)	119 (73.0)	17.3 (7.5, NE)	0.6248 (0.4339, 0.8997)	0.0108 (0.0115)
Negative	42	9 (21.4)	33 (78.6)	NE (11.6, NE)	21	3 (14.3)	18 (85.7)	NE (5.3, NE)	0.6805 (0.1716, 2.6976)	0.5779 (0.5838)

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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EQ-5D-5L VAS

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (derived)										0.6672
Positive	333	94 (28.2)	239 (71.8)	21.7 (18.1, NE)	166	44 (26.5)	122 (73.5)	17.3 (8.4, NE)	0.6235 (0.4325, 0.8987)	0.0106 (0.0113)
Negative	40	10 (25.0)	30 (75.0)	17.8 (11.6, NE)	18	3 (16.7)	15 (83.3)	NE (5.3, NE)	0.7418 (0.1937, 2.8400)	0.6579 (0.6627)

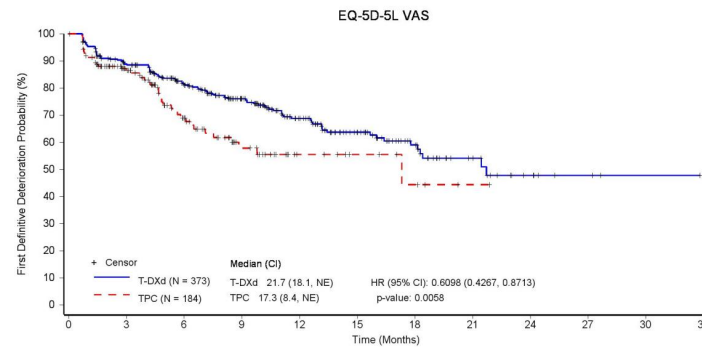
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Run date: 15SEP2022 – 11:59; Program name: T3\_EQ5D\_FD\_2\_FAS.sas; Output name: T3\_EQ5D\_DD\_2\_FAS.rtf

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DE.F.3.2.3 - EQ-5D-5L VAS - Definitive deterioration - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	288	223	170	109	69	40	19	7	3	1	0
TPC (N = 184)	184	107	54	27	11	7	4	1	0	0	0	0

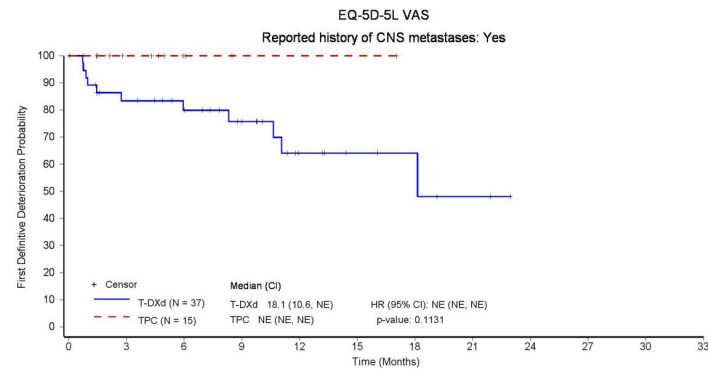
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:11; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F3\_EQ5D\_DD\_3\_FAS.rtf



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Patients still at risk:

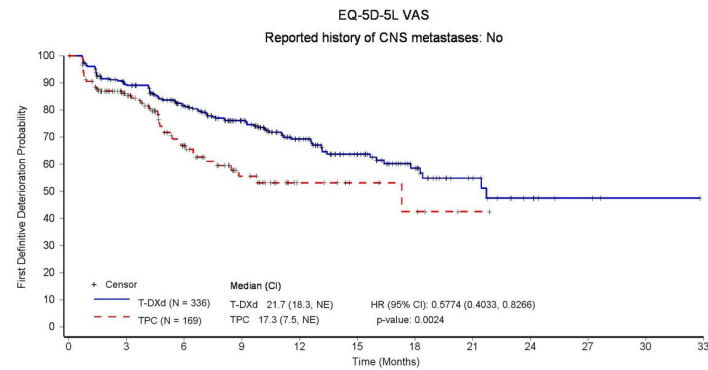
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 37)	37	28	23	17	8	5	4	2	0	0	0	0
TPC (N = 15)	15	8	3	1	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

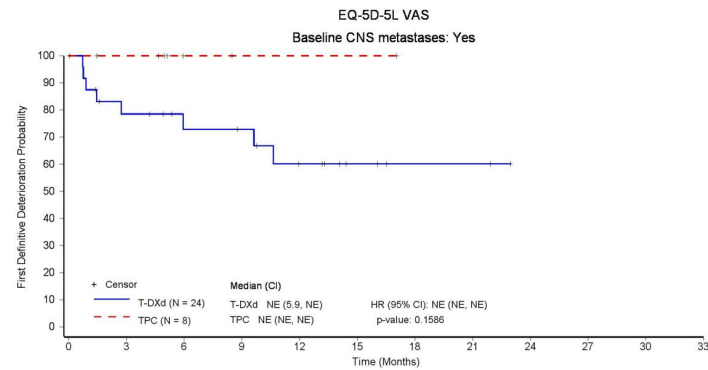
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 336)	336	260	200	153	101	64	36	17	7	3	1	0
TPC (N = 169)	169	99	51	26	10	6	4	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:11; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EQ5D\_DD\_4\_FAS.rtf

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Patients still at risk:

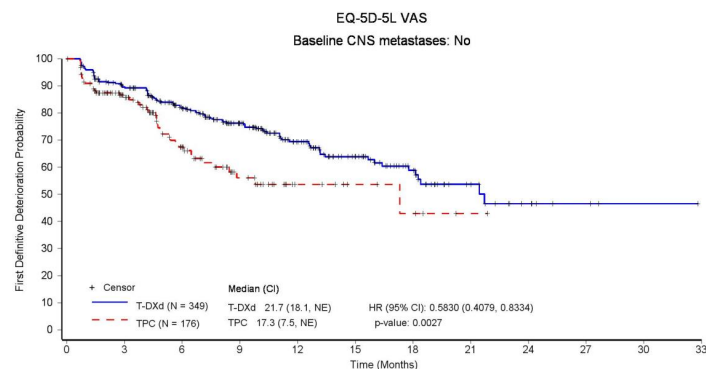
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 24)	24	17	13	12	8	4	2	2	0	0	0	0
TPC (N = 8)	8	6	2	1	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:11; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EQ5D\_DD\_4\_FAS.rtf

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Patients still at risk:

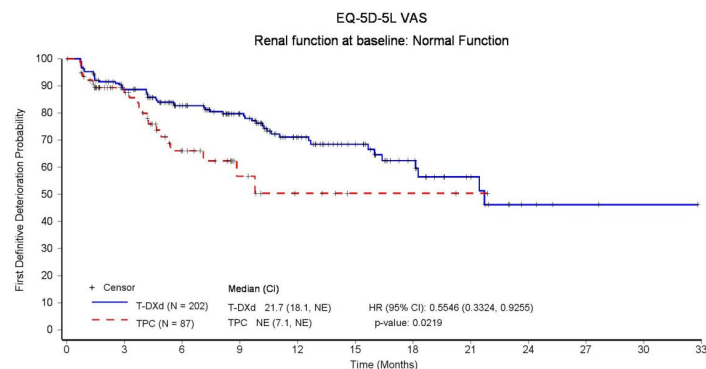
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 349)	349	271	210	158	101	65	38	17	7	3	1	0
TPC (N = 176)	176	101	52	26	10	6	4	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:11; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EQ5D\_DD\_4\_FAS.rtf

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Patients still at risk:

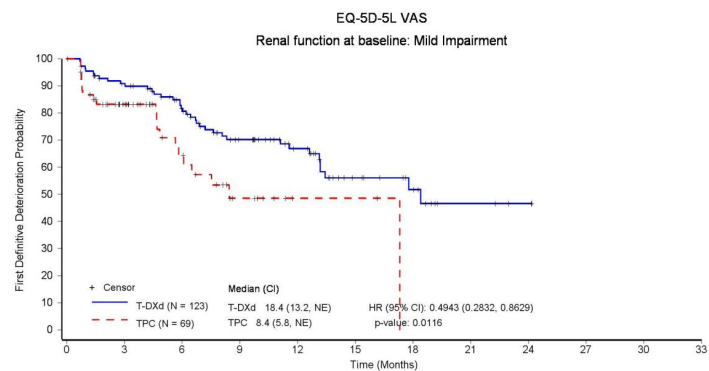
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 202)	202	158	121	93	57	40	23	12	4	2	1	0
TPC (N = 87)	87	48	22	10	5	2	2	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:11; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EQ5D\_DD\_4\_FAS.rtf

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Patients still at risk:

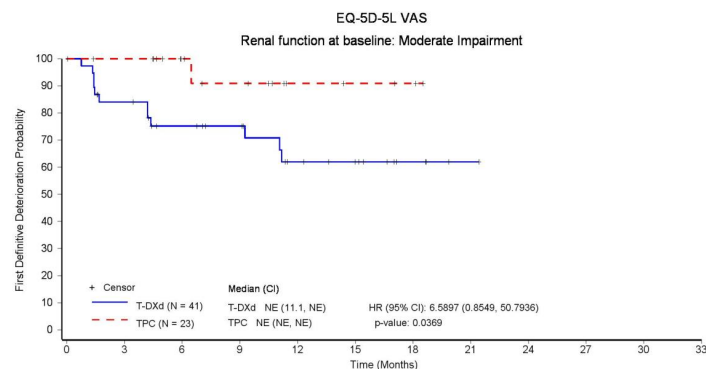
T-DXd (N = 123)	123	95	76	54	38	19	12	5	2	0	0	0
TPC (N = 69)	69	38	20	8	2	2	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:11; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EQ5D\_DD\_4\_FAS.rtf

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Patients still at risk:

T-DXd (N = 41)	41	30	23	20	12	9	4	1	0	0	0	0
TPC (N = 23)	23	19	12	9	4	3	2	0	0	0	0	0

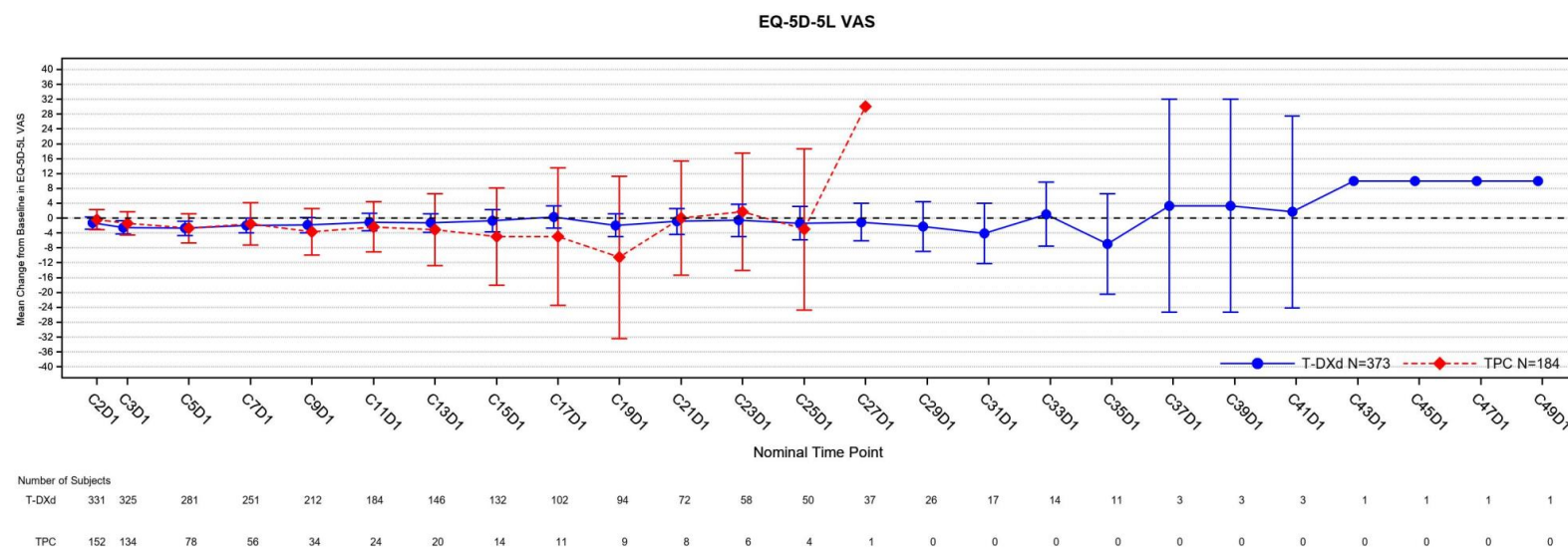
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:11; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EQ5D\_DD\_4\_FAS.rtf

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DE.F.3.3.1 - EQ-5D-5L VAS - Mean change from baseline plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Number of subjects is number of subjects with an observation at the visit (i.e. scale score calculable for the visit). Error bars represent the 95% confidence interval for the mean value. A high score for EORTC-QLQ-C30 global health status represents a low/unhealthy level of functioning; a high score for a EORTC-QLQ-C30 and EORTC-QLQ-BR45 symptom scale/item represents a high level of symptomology/problems; a high score for a EORTC-QLQ-C30 and EORTC-QLQ-BR45 functional scale represents a low/unhealthy level of functioning A high score for the EQ-5D-5L VAS represents a low/unhealthy level of functioning;

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.3.4.1 - EQ-5D-5L VAS - Mixed Model for Repeated Measurement - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

EQ-5D-5L VAS\*

Parameter	n[a]	Estimate [b]	Standard Error	P-value
Intercept		-5.11	2.370	0.0315
Treatment				
T-DXd	346	-1.11	1.500	0.4588
TPC	162	0		
Time of Visit		0.01	0.004	0.0002
Treatment*Time of Visit		-0.01	0.004	0.0726

A negative estimate denotes an improvement in health status in terms of the scale/item being evaluated.

[a] n is the number of subjects included in the model in each treatment group.

[b] Estimates obtained from a mixed model including terms for treatment, the randomization stratification factors, time of visit (days), and treatment-by-time of visit interaction as well as the intercept as random effect.

\* Unstructured covariance matrix was used to model the correlation within subject; † AR(1) covariance structure used to model correlation within subjects; ‡ Compound symmetry covariance structure used to model correlation within subjects

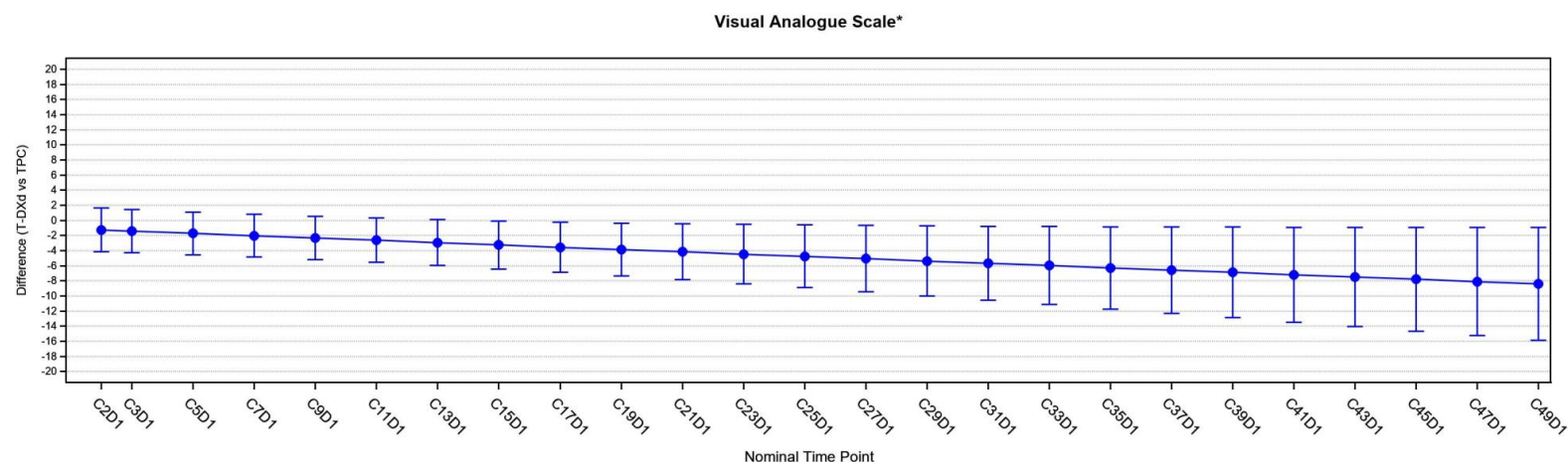
Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 15SEP2022 – 12:00; Program name: T3\_EQ5D\_MMRM\_1\_FAS.sas; Output name: T3\_EQ5D\_MMRM\_1\_FAS.rtf

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DE.F.3.4.2 - EQ-5D-5L VAS - Plot of least-square means of repeated measures analysis of change from baseline - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Least square mean (LSM) estimates of trastuzumab deruxtecan versus comparator and their 95% CI are calculated using a restricted maximum likelihood (REML) based mixed model including terms for treatment, the randomization stratification factors, time of visit (days), and treatment by time of visit interaction as well as the intercept as random effect. A high score for global health status represents a low quality of life (change of direction from raw score); a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomology/problems.

\* Unstructured covariance matrix was used to model the correlation within subject. † AR(1) covariance structure used to model correlation within subjects. ‡ Compound symmetry covariance structure used to model correlation within subjects

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 15SEP2022 – 12:00; Program name: F3\_EQ5D\_MMRM\_2\_FAS.sas; Output name: F3\_EQ5D\_MMRM\_2\_FAS.rtf

**Anhang 4-G 3.2: EORTC QLQ-C30 (MID 15 Punkte)**

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DE.T.3.5.1 - EORTC QLQ-C30 - First deterioration - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

#### Global Health Status

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	210 (56.3)	99 (53.8)	
Number of subjects censored, n (%)	163 (43.7)	85 (46.2)	
Median time to first event (months) [a]	5.1	4.2	
95% Confidence Interval	[4.2, 7.0]	[2.8, 5.9]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.8224
95% Confidence Interval			[0.6449, 1.0488]
p-value			0.1150
Stratified log-rank p-value [c]			0.1103

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
Run date: 15SEP2022 – 12:00; Program name: T3\_EQ5D\_FD\_1\_FAS.sas; Output name: T3\_EORTCC30\_FD\_1\_FAS.rtf

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Functional Scales/Physical Functioning

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	131 (35.1)	70 (38.0)	
Number of subjects censored, n (%)	242 (64.9)	114 (62.0)	
Median time to first event (months) [a] 95% Confidence Interval	NE [13.9, NE]	8.4 [5.9, 11.3]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.6217 [0.4614, 0.8377] 0.0018
Stratified log-rank p-value [c]			0.0016

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 15SEP2022 – 12:00; Program name: T3\_EQ5D\_FD\_1\_FAS.sas; Output name: T3\_EORTCC30\_FD\_1\_FAS.rtf

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Functional Scales/Role Functioning

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	217 (58.2)	106 (57.6)	
Number of subjects censored, n (%)	156 (41.8)	78 (42.4)	
Median time to first event (months) [a]	4.2	2.9	
95% Confidence Interval	[2.9, 5.7]	[1.5, 4.3]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.7648
95% Confidence Interval			[0.6032, 0.9698]
p-value			0.0269
Stratified log-rank p-value [c]			0.0257

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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#### Functional Scales/Emotional Functioning

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	170 (45.6)	71 (38.6)	
Number of subjects censored, n (%)	203 (54.4)	113 (61.4)	
Median time to first event (months) [a]	11.1	7.0	
95% Confidence Interval	[8.5, 13.6]	[5.7, 10.2]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.8192
95% Confidence Interval			[0.6165, 1.0884]
p-value			0.1689
Stratified log-rank p-value [c]			0.1628

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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#### Functional Scales/Cognitive Functioning

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	205 (55.0)	97 (52.7)	
Number of subjects censored, n (%)	168 (45.0)	87 (47.3)	
Median time to first event (months) [a]	6.2	4.4	
95% Confidence Interval	[4.7, 7.7]	[3.3, 6.3]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.7820
95% Confidence Interval			[0.6094, 1.0035]
p-value			0.0533
Stratified log-rank p-value [c]			0.0493

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Functional Scales/Social Functioning

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	211 (56.6)	107 (58.2)	
Number of subjects censored, n (%)	162 (43.4)	77 (41.8)	
Median time to first event (months) [a]	5.9	3.8	
95% Confidence Interval	[4.2, 9.7]	[2.7, 4.7]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.7183
95% Confidence Interval			[0.5656, 0.9123]
p-value			0.0067
Stratified log-rank p-value [c]			0.0064

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Symptom Scales/Fatigue

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	176 (47.2)	80 (43.5)	
Number of subjects censored, n (%)	197 (52.8)	104 (56.5)	
Median time to first event (months) [a]	10.6	5.9	
95% Confidence Interval	[7.5, 13.9]	[4.0, 11.4]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.8148
95% Confidence Interval			[0.6217, 1.0680]
p-value			0.1380
Stratified log-rank p-value [c]			0.1333

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 15SEP2022 – 12:00; Program name: T3\_EQ5D\_FD\_1\_FAS.sas; Output name: T3\_EORTCC30\_FD\_1\_FAS.rtf

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DE.T.3.5.1 - EORTC QLQ-C30 - First deterioration - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Symptom Scales/Nausea and Vomiting

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	258 (69.2)	73 (39.7)	
Number of subjects censored, n (%)	115 (30.8)	111 (60.3)	
Median time to first event (months) [a]	1.5	8.2	
95% Confidence Interval	[1.4, 1.7]	[6.0, 9.8]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			2.0765
95% Confidence Interval			[1.5976, 2.6990]
p-value			<0.0001
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Symptom Scales/Pain

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	188 (50.4)	97 (52.7)	
Number of subjects censored, n (%)	185 (49.6)	87 (47.3)	
Median time to first event (months) [a]	9.2	4.4	
95% Confidence Interval	[7.1, 11.1]	[2.7, 6.1]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.6239
95% Confidence Interval			[0.4848, 0.8031]
p-value			0.0002
Stratified log-rank p-value [c]			0.0002

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Common Symptoms/Dyspnoea

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	164 (44.0)	74 (40.2)	
Number of subjects censored, n (%)	209 (56.0)	110 (59.8)	
Median time to first event (months) [a]	12.5	6.7	
95% Confidence Interval	[8.3, 20.9]	[5.1, 13.7]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.7950
95% Confidence Interval			[0.6003, 1.0528]
p-value			0.1094
Stratified log-rank p-value [c]			0.1092

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Common Symptoms/Insomnia

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	149 (39.9)	85 (46.2)	
Number of subjects censored, n (%)	224 (60.1)	99 (53.8)	
Median time to first event (months) [a]	16.0	5.4	
95% Confidence Interval	[10.6, 18.6]	[4.2, 7.0]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.5237
95% Confidence Interval			[0.3970, 0.6907]
p-value			<0.0001
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Common Symptoms/Appetite Loss

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	215 (57.6)	80 (43.5)	
Number of subjects censored, n (%)	158 (42.4)	104 (56.5)	
Median time to first event (months) [a]	5.1	6.5	
95% Confidence Interval	[3.5, 7.2]	[5.0, 9.8]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			1.1907
95% Confidence Interval			[0.9179, 1.5445]
p-value			0.1887
Stratified log-rank p-value [c]			0.1976

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Common Symptoms/Constipation

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	219 (58.7)	82 (44.6)	
Number of subjects censored, n (%)	154 (41.3)	102 (55.4)	
Median time to first event (months) [a]	4.2	5.9	
95% Confidence Interval	[2.9, 5.6]	[4.4, 8.4]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			1.1240
95% Confidence Interval			[0.8682, 1.4551]
p-value			0.3749
Stratified log-rank p-value [c]			0.3794

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Common Symptoms/Diarrhea

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	173 (46.4)	56 (30.4)	
Number of subjects censored, n (%)	200 (53.6)	128 (69.6)	
Median time to first event (months) [a]	9.6	13.3	
95% Confidence Interval	[7.0, 16.1]	[9.0, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			1.4167
95% Confidence Interval			[1.0442, 1.9220]
p-value			0.0252
Stratified log-rank p-value [c]			0.0254

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Common Symptoms/Financial Difficulties

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	106 (28.4)	48 (26.1)	
Number of subjects censored, n (%)	267 (71.6)	136 (73.9)	
Median time to first event (months) [a]	NE	18.5	
95% Confidence Interval	[NE, NE]	[11.3, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.7699
95% Confidence Interval			[0.5421, 1.0935]
p-value			0.1441
Stratified log-rank p-value [c]			0.1405

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Global Health Status

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.5496
HER2 IHC 1+	214	125 (58.4)	89 (41.6)	4.3 (2.8, 5.7)	107	58 (54.2)	49 (45.8)	4.2 (2.7, 5.9)	0.8777 (0.6416, 1.2005)	0.4014	
HER2 IHC 2+/ISH Negative	159	85 (53.5)	74 (46.5)	7.2 (4.2, 12.7)	77	41 (53.2)	36 (46.8)	3.7 (2.0, 7.7)	0.7405 (0.5076, 1.0803)	0.1158	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Global Health Status

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.6031
1	221	133 (60.2)	88 (39.8)	4.2 (2.8, 5.7)	100	54 (54.0)	46 (46.0)	3.5 (1.7, 7.7)	0.8609 (0.6258, 1.1842) 0.3572	0.3519
>=2	151	76 (50.3)	75 (49.7)	6.9 (4.9, 13.1)	83	45 (54.2)	38 (45.8)	4.5 (2.8, 6.9)	0.7303 (0.5035, 1.0593) 0.0976	0.0931

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Global Health Status

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.8876
Yes	235	130 (55.3)	105 (44.7)	4.3 (2.9, 8.1)	118	61 (51.7)	57 (48.3)	4.0 (2.7, 6.9)	0.8139 (0.5982, 1.1073) 0.1898	0.1806	
No	98	60 (61.2)	38 (38.8)	5.7 (4.2, 8.5)	48	28 (58.3)	20 (41.7)	3.9 (1.7, 9.7)	0.8342 (0.5322, 1.3077) 0.4294	0.4300	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Global Health Status

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5479
<65	290	160 (55.2)	130 (44.8)	5.7 (4.2, 8.6)	136	69 (50.7)	67 (49.3)	4.2 (2.8, 5.9)	0.7932 (0.5963, 1.0553) 0.1117	0.1061	
>=65	83	50 (60.2)	33 (39.8)	3.4 (1.7, 5.8)	48	30 (62.5)	18 (37.5)	3.7 (1.5, 7.7)	0.9513 (0.6042, 1.4976) 0.8291	0.8262	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Global Health Status

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											0.9107
<75	359	202 (56.3)	157 (43.7)	5.2 (4.1, 7.2)	175	93 (53.1)	82 (46.9)	4.2 (2.8, 5.9)	0.8101 (0.6322, 1.0381) 0.0961	0.0904	
>=75	14	8 (57.1)	6 (42.9)	4.4 (1.6, NE)	9	6 (66.7)	3 (33.3)	3.7 (0.7, NE)	0.8214 (0.2838, 2.3779) 0.7168	0.7205	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Global Health Status

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.3688
White	176	88 (50.0)	88 (50.0)	6.3 (3.9, 14.4)	91	45 (49.5)	46 (50.5)	4.0 (2.7, 8.6)	0.7406 (0.5153, 1.0645) 0.1047	0.1018	
Non-White	197	122 (61.9)	75 (38.1)	4.7 (2.9, 5.9)	92	53 (57.6)	39 (42.4)	4.2 (2.0, 6.9)	0.8898 (0.6431, 1.2311) 0.4810	0.4698	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Global Health Status

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.5240
Asia	147	100 (68.0)	47 (32.0)	4.2 (2.8, 5.7)	66	40 (60.6)	26 (39.4)	2.4 (1.5, 5.9)	0.9217 (0.6374, 1.3329) 0.6649	0.6529	
North America	60	26 (43.3)	34 (56.7)	6.3 (2.3, NE)	33	16 (48.5)	17 (51.5)	3.7 (1.5, 8.6)	0.6184 (0.3271, 1.1691) 0.1391	0.1343	
Europe + Israel	166	84 (50.6)	82 (49.4)	5.9 (4.2, 12.7)	85	43 (50.6)	42 (49.4)	4.5 (3.1, 9.0)	0.7854 (0.5426, 1.1369) 0.2005	0.1959	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Global Health Status

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.7630
0	200	125 (62.5)	75 (37.5)	4.3 (2.9, 5.7)	105	57 (54.3)	48 (45.7)	3.5 (2.1, 5.4)	0.8465 (0.6177, 1.1601) 0.3001	0.2964	
1	173	85 (49.1)	88 (50.9)	7.6 (4.2, 14.4)	79	42 (53.2)	37 (46.8)	5.1 (2.4, 8.4)	0.7685 (0.5287, 1.1172) 0.1678	0.1606	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Global Health Status

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.1744
0	60	38 (63.3)	22 (36.7)	4.2 (2.7, 6.3)	34	19 (55.9)	15 (44.1)	4.5 (1.7, 5.9)	0.8528 (0.4893, 1.4864) 0.5744	0.5783
1	108	58 (53.7)	50 (46.3)	5.8 (2.8, 13.1)	51	23 (45.1)	28 (54.9)	7.7 (2.3, NE)	1.1165 (0.6884, 1.8111) 0.6551	0.6559
2	115	55 (47.8)	60 (52.2)	8.8 (4.3, NE)	54	32 (59.3)	22 (40.7)	3.7 (2.7, 6.9)	0.5448 (0.3480, 0.8529) 0.0079	0.0063

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Global Health Status

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	59 (65.6)	31 (34.4)	4.2 (2.8, 5.7)	45	25 (55.6)	20 (44.4)	2.8 (1.5, NE)	0.8811 (0.5499, 1.4118) 0.5988	0.5882	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Global Health Status

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.2514
PD	174	80 (46.0)	94 (54.0)	8.6 (4.7, 18.2)	85	42 (49.4)	43 (50.6)	5.3 (2.8, 7.5)	0.6639 (0.4548, 0.9691) 0.0338	0.0317	
PR	48	34 (70.8)	14 (29.2)	2.8 (1.4, 7.9)	22	10 (45.5)	12 (54.5)	3.9 (1.5, NE)	1.2856 (0.6318, 2.6160) 0.4882	0.5128	
SD	82	50 (61.0)	32 (39.0)	4.8 (2.8, 8.5)	55	36 (65.5)	19 (34.5)	2.8 (1.6, 5.1)	0.7147 (0.4636, 1.1019) 0.1284	0.1280	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Global Health Status

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Reported history of CNS metastases											0.3376
Yes	37	20 (54.1)	17 (45.9)	5.7 (2.9, NE)	15	4 (26.7)	11 (73.3)	NE (0.9, NE)	1.2719 (0.4334, 3.7325)	0.6617	
No	336	190 (56.5)	146 (43.5)	4.8 (3.9, 6.9)	169	95 (56.2)	74 (43.8)	3.9 (2.8, 5.8)	0.7969 (0.6214, 1.0218)	0.0689	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Global Health Status

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.0352
Yes	24	14 (58.3)	10 (41.7)	8.8 (1.4, NE)	8	1 (12.5)	7 (87.5)	NE (1.7, NE)	4.1172 (0.5375, 31.5378) 0.1731	0.1401
No	349	196 (56.2)	153 (43.8)	4.8 (3.9, 6.9)	176	98 (55.7)	78 (44.3)	3.9 (2.7, 5.4)	0.7807 (0.6113, 0.9971) 0.0473	0.0441

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.4396
Normal Function	202	103 (51.0)	99 (49.0)	5.7 (4.2, 18.2)	87	44 (50.6)	43 (49.4)	4.2 (3.0, 5.9)	0.7668 (0.5361, 1.0968) 0.1460	0.1353	
Mild Impairment	123	80 (65.0)	43 (35.0)	3.9 (2.8, 5.7)	69	39 (56.5)	30 (43.5)	2.8 (1.7, 8.4)	0.8479 (0.5763, 1.2476) 0.4024	0.3955	
Moderate Impairment	41	23 (56.1)	18 (43.9)	5.7 (1.6, NE)	23	12 (52.2)	11 (47.8)	7.7 (1.4, NE)	1.1962 (0.5946, 2.4068) 0.6155	0.6129	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.4134
Normal Function	170	106 (62.4)	64 (37.6)	4.5 (2.8, 5.7)	98	56 (57.1)	42 (42.9)	4.5 (2.8, 7.5)	0.9156 (0.6611, 1.2682) 0.5959	0.5753	
Mild Impairment	195	102 (52.3)	93 (47.7)	5.8 (3.9, 8.8)	84	41 (48.8)	43 (51.2)	3.9 (2.0, 8.6)	0.7767 (0.5382, 1.1209) 0.1770	0.1741	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Baseline visceral disease											0.2189
Yes	332	181 (54.5)	151 (45.5)	5.6 (4.2, 8.1)	157	83 (52.9)	74 (47.1)	3.7 (2.7, 7.0)	0.7814 (0.6013, 1.0156) 0.0651	0.0622	
No	41	29 (70.7)	12 (29.3)	2.8 (1.6, 6.3)	27	16 (59.3)	11 (40.7)	5.3 (1.5, 5.9)	1.1390 (0.6172, 2.1021) 0.6771	0.6862	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Global Health Status

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.9811
Positive	331	189 (57.1)	142 (42.9)	5.1 (4.1, 7.0)	163	86 (52.8)	77 (47.2)	4.0 (2.7, 6.9)	0.8223 (0.6360, 1.0632)	0.1299	
Negative	42	21 (50.0)	21 (50.0)	4.7 (2.2, NE)	21	13 (61.9)	8 (38.1)	4.4 (1.7, 9.9)	0.7858 (0.3894, 1.5858)	0.5013	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Global Health Status

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.8760
Positive	333	190 (57.1)	143 (42.9)	5.1 (4.1, 7.0)	166	89 (53.6)	77 (46.4)	4.0 (2.7, 5.9)	0.8149 (0.6322, 1.0504) 0.1140	0.1084	
Negative	40	20 (50.0)	20 (50.0)	4.7 (2.7, NE)	18	10 (55.6)	8 (44.4)	5.3 (1.7, 9.9)	0.8348 (0.3866, 1.8027) 0.6457	0.6439	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]	
HER2 status										0.3998	
HER2 IHC 1+	214	78 (36.4)	136 (63.6)	18.7 (11.3, NE)	107	38 (35.5)	69 (64.5)	8.5 (5.4, NE)	0.7095 (0.4781, 1.0527)	0.0860	
HER2 IHC 2+/ISH Negative	159	53 (33.3)	106 (66.7)	NE (13.1, NE)	77	32 (41.6)	45 (58.4)	7.5 (5.3, 14.7)	0.5227 (0.3351, 0.8154)	0.0036	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.9362
1	221	73 (33.0)	148 (67.0)	NE (13.4, NE)	100	36 (36.0)	64 (64.0)	10.1 (6.3, 16.9)	0.6182 (0.4120, 0.9276)	0.0193
>=2	151	58 (38.4)	93 (61.6)	18.7 (8.7, NE)	83	34 (41.0)	49 (59.0)	6.1 (4.5, NE)	0.6304 (0.4097, 0.9698)	0.0337

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Prior CDK4/6											
Yes	235	76 (32.3)	159 (67.7)	NE (13.9, NE)	118	39 (33.1)	79 (66.9)	8.6 (6.3, 16.9)	0.6600 (0.4459, 0.9770)	0.0364	0.4352
No	98	41 (41.8)	57 (58.2)	18.7 (9.2, NE)	48	25 (52.1)	23 (47.9)	6.1 (4.2, 9.7)	0.5116 (0.3083, 0.8490)	0.0083	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8768
<65	290	104 (35.9)	186 (64.1)	NE (12.0, NE)	136	51 (37.5)	85 (62.5)	7.9 (5.7, 14.7)	0.6173 (0.4388, 0.8686) 0.0056	0.0051	
>=65	83	27 (32.5)	56 (67.5)	18.7 (15.2, NE)	48	19 (39.6)	29 (60.4)	9.7 (4.5, NE)	0.6064 (0.3343, 1.1001) 0.0998	0.0979	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4412
<75	359	129 (35.9)	230 (64.1)	18.7 (13.4, NE)	175	66 (37.7)	109 (62.3)	7.9 (5.8, 10.1)	0.6188 (0.4574, 0.8372) 0.0019	0.0017	
>=75	14	2 (14.3)	12 (85.7)	NE (3.4, NE)	9	4 (44.4)	5 (55.6)	11.3 (1.4, NE)	0.3488 (0.0638, 1.9056) 0.2241	0.2032	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Race									0.4902	
White	176	60 (34.1)	116 (65.9)	NE (11.1, NE)	91	30 (33.0)	61 (67.0)	8.6 (5.1, NE)	0.7053 (0.4525, 1.0994)	0.1225
Non-White	197	71 (36.0)	126 (64.0)	18.7 (13.4, NE)	92	40 (43.5)	52 (56.5)	7.5 (5.8, 11.3)	0.5451 (0.3662, 0.8113)	0.0024

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.5409
Asia	147	58 (39.5)	89 (60.5)	16.9 (12.0, NE)	66	29 (43.9)	37 (56.1)	8.4 (5.4, 14.7)	0.6012 (0.3814, 0.9477) 0.0284	0.0264	
North America	60	14 (23.3)	46 (76.7)	NE (11.2, NE)	33	11 (33.3)	22 (66.7)	7.9 (2.0, NE)	0.4258 (0.1895, 0.9565) 0.0387	0.0338	
Europe + Israel	166	59 (35.5)	107 (64.5)	18.7 (11.1, NE)	85	30 (35.3)	55 (64.7)	8.6 (5.1, NE)	0.7122 (0.4561, 1.1122) 0.1356	0.1339	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.4819
0	200	62 (31.0)	138 (69.0)	NE (16.9, NE)	105	35 (33.3)	70 (66.7)	9.7 (5.7, NE)	0.5578 (0.3662, 0.8497) 0.0066	0.0058	
1	173	69 (39.9)	104 (60.1)	15.2 (8.3, NE)	79	35 (44.3)	44 (55.7)	7.5 (4.7, 10.1)	0.6892 (0.4553, 1.0431) 0.0783	0.0760	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.9633
0	60	23 (38.3)	37 (61.7)	NE (6.2, NE)	34	12 (35.3)	22 (64.7)	5.9 (4.5, NE)	0.6743 (0.3314, 1.3721) 0.2769	0.2749	
1	108	36 (33.3)	72 (66.7)	16.9 (12.0, NE)	51	20 (39.2)	31 (60.8)	11.3 (4.6, NE)	0.6492 (0.3736, 1.1279) 0.1253	0.1227	
2	115	36 (31.3)	79 (68.7)	NE (NE, NE)	54	19 (35.2)	35 (64.8)	7.5 (5.1, NE)	0.6154 (0.3498, 1.0826) 0.0921	0.0881	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	36 (40.0)	54 (60.0)	13.9 (8.3, NE)	45	19 (42.2)	26 (57.8)	8.4 (3.0, 14.7)	0.6295 (0.3573, 1.1093) 0.1094	0.1066	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.9160
PD	174	54 (31.0)	120 (69.0)	18.7 (13.4, NE)	85	29 (34.1)	56 (65.9)	7.7 (5.4, NE)	0.5567 (0.3500, 0.8854) 0.0134	0.0121	
PR	48	23 (47.9)	25 (52.1)	16.9 (4.4, NE)	22	9 (40.9)	13 (59.1)	4.7 (3.8, NE)	0.7101 (0.3243, 1.5549) 0.3919	0.3795	
SD	82	28 (34.1)	54 (65.9)	NE (11.2, NE)	55	23 (41.8)	32 (58.2)	8.6 (5.1, 16.9)	0.6374 (0.3646, 1.1144) 0.1141	0.1106	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.4558
Yes	37	15 (40.5)	22 (59.5)	NE (3.0, NE)	15	4 (26.7)	11 (73.3)	NE (0.8, NE)	1.0150 (0.3343, 3.0812) 0.9791	0.9794
No	336	116 (34.5)	220 (65.5)	NE (13.9, NE)	169	66 (39.1)	103 (60.9)	7.9 (5.8, 11.3)	0.5867 (0.4312, 0.7982) 0.0007	0.0006

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.3208
Yes	24	10 (41.7)	14 (58.3)	NE (4.9, NE)	8	2 (25.0)	6 (75.0)	NE (0.7, NE)	1.2335 (0.2682, 5.6738) 0.7875	0.7805
No	349	121 (34.7)	228 (65.3)	NE (13.9, NE)	176	68 (38.6)	108 (61.4)	7.9 (5.8, 11.3)	0.5911 (0.4368, 0.7999) 0.0007	0.0006

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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## Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Renal function at baseline										0.0068
Normal Function	202	61 (30.2)	141 (69.8)	NE (16.9, NE)	87	36 (41.4)	51 (58.6)	6.3 (4.7, 10.1)	0.4361 (0.2854, 0.6663) 0.0001	<0.0001
Mild Impairment	123	49 (39.8)	74 (60.2)	13.9 (8.3, NE)	69	26 (37.7)	43 (62.3)	7.9 (5.7, 16.9)	0.6547 (0.4014, 1.0677) 0.0896	0.0872
Moderate Impairment	41	19 (46.3)	22 (53.7)	9.1 (4.2, NE)	23	6 (26.1)	17 (73.9)	NE (11.3, NE)	1.9211 (0.7616, 4.8462) 0.1667	0.1594

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.6296
Normal Function	170	66 (38.8)	104 (61.2)	16.9 (11.2, NE)	98	43 (43.9)	55 (56.1)	7.5 (4.6, 14.7)	0.5848 (0.3962, 0.8631) 0.0069	0.0062
Mild Impairment	195	64 (32.8)	131 (67.2)	NE (13.1, NE)	84	27 (32.1)	57 (67.9)	8.6 (5.3, 16.9)	0.6820 (0.4314, 1.0781) 0.1014	0.0993

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1491
Yes	332	118 (35.5)	214 (64.5)	18.7 (13.4, NE)	157	57 (36.3)	100 (63.7)	8.6 (6.3, 14.7)	0.6751 (0.4901, 0.9299) 0.0162	0.0155	
No	41	13 (31.7)	28 (68.3)	NE (9.2, NE)	27	13 (48.1)	14 (51.9)	5.3 (4.3, NE)	0.3721 (0.1667, 0.8304) 0.0158	0.0123	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.7429
Positive	331	116 (35.0)	215 (65.0)	18.7 (13.4, NE)	163	62 (38.0)	101 (62.0)	8.4 (6.1, 11.3)	0.6047 (0.4421, 0.8271) 0.0016	0.0015	
Negative	42	15 (35.7)	27 (64.3)	NE (4.7, NE)	21	8 (38.1)	13 (61.9)	5.9 (4.4, NE)	0.7804 (0.3260, 1.8678) 0.5776	0.5725	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.4961
Positive	333	116 (34.8)	217 (65.2)	18.7 (13.9, NE)	166	64 (38.6)	102 (61.4)	8.4 (5.8, 11.3)	0.5929 (0.4347, 0.8085) 0.0010	0.0008	
Negative	40	15 (37.5)	25 (62.5)	NE (4.7, NE)	18	6 (33.3)	12 (66.7)	NE (4.5, NE)	0.9247 (0.3545, 2.4118) 0.8729	0.8736	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.2945
HER2 IHC 1+	214	121 (56.5)	93 (43.5)	4.3 (2.8, 5.9)	107	62 (57.9)	45 (42.1)	2.9 (1.4, 4.3)	0.6636 (0.4866, 0.9051) 0.0096	0.0093	
HER2 IHC 2+/ISH Negative	159	96 (60.4)	63 (39.6)	4.2 (2.8, 6.3)	77	44 (57.1)	33 (42.9)	2.9 (1.5, 6.1)	0.8454 (0.5901, 1.2112) 0.3600	0.3520	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.7569
1	221	134 (60.6)	87 (39.4)	4.2 (2.8, 5.6)	100	59 (59.0)	41 (41.0)	2.1 (1.4, 4.3)	0.7598 (0.5585, 1.0338) 0.0804	0.0795	
>=2	151	82 (54.3)	69 (45.7)	5.6 (2.8, 8.4)	83	47 (56.6)	36 (43.4)	2.9 (1.6, 4.7)	0.6965 (0.4834, 1.0036) 0.0523	0.0488	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.3747
Yes	235	133 (56.6)	102 (43.4)	4.2 (2.9, 6.2)	118	65 (55.1)	53 (44.9)	2.9 (1.5, 4.4)	0.7678 (0.5693, 1.0357) 0.0835	0.0798	
No	98	62 (63.3)	36 (36.7)	5.1 (2.8, 7.5)	48	32 (66.7)	16 (33.3)	1.5 (1.2, 4.3)	0.5960 (0.3867, 0.9183) 0.0190	0.0185	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3618
<65	290	160 (55.2)	130 (44.8)	4.6 (3.5, 6.9)	136	75 (55.1)	61 (44.9)	3.2 (1.5, 4.4)	0.6988 (0.5292, 0.9227) 0.0115	0.0108	
>=65	83	57 (68.7)	26 (31.3)	2.8 (1.5, 4.2)	48	31 (64.6)	17 (35.4)	1.9 (1.4, 4.7)	0.8901 (0.5731, 1.3823) 0.6042	0.6085	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8785
<75	359	209 (58.2)	150 (41.8)	4.3 (2.9, 5.8)	175	100 (57.1)	75 (42.9)	2.9 (1.5, 4.4)	0.7320 (0.5753, 0.9315) 0.0112	0.0105	
>=75	14	8 (57.1)	6 (42.9)	2.8 (1.6, NE)	9	6 (66.7)	3 (33.3)	2.8 (0.7, NE)	0.8068 (0.2794, 2.3302) 0.6916	0.6757	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.1981
White	176	99 (56.3)	77 (43.8)	2.9 (2.8, 5.6)	91	46 (50.5)	45 (49.5)	3.8 (1.5, 4.8)	0.8927 (0.6278, 1.2692)	0.5229 (0.5272)	
Non-White	197	118 (59.9)	79 (40.1)	4.6 (3.3, 6.7)	92	60 (65.2)	32 (34.8)	2.0 (1.4, 3.7)	0.6222 (0.4543, 0.8523)	0.0028 (0.0031)	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.2350
Asia	147	90 (61.2)	57 (38.8)	4.6 (4.2, 6.9)	66	46 (69.7)	20 (30.3)	2.1 (1.4, 4.4)	0.6092 (0.4253, 0.8726) 0.0069	0.0064	
North America	60	27 (45.0)	33 (55.0)	4.1 (1.6, NE)	33	17 (51.5)	16 (48.5)	2.0 (1.4, 4.5)	0.6687 (0.3608, 1.2391) 0.2010	0.1943	
Europe + Israel	166	100 (60.2)	66 (39.8)	2.9 (2.8, 5.9)	85	43 (50.6)	42 (49.4)	3.8 (1.5, 5.8)	0.9416 (0.6574, 1.3486) 0.7427	0.7332	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.8635
0	200	118 (59.0)	82 (41.0)	4.3 (2.9, 6.3)	105	58 (55.2)	47 (44.8)	2.8 (1.5, 4.5)	0.7272 (0.5298, 0.9982) 0.0487	0.0474	
1	173	99 (57.2)	74 (42.8)	4.2 (2.8, 6.2)	79	48 (60.8)	31 (39.2)	2.9 (1.5, 4.5)	0.7472 (0.5268, 1.0600) 0.1024	0.0987	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.2458
0	60	40 (66.7)	20 (33.3)	2.8 (1.4, 3.3)	34	17 (50.0)	17 (50.0)	4.5 (1.5, 5.9)	1.0841 (0.6113, 1.9226) 0.7824	0.7835	
1	108	57 (52.8)	51 (47.2)	4.4 (2.8, 12.5)	51	28 (54.9)	23 (45.1)	3.2 (1.4, 6.1)	0.7725 (0.4910, 1.2154) 0.2643	0.2594	
2	115	60 (52.2)	55 (47.8)	5.9 (4.2, 11.8)	54	33 (61.1)	21 (38.9)	2.1 (1.4, 3.7)	0.5439 (0.3516, 0.8414) 0.0062	0.0050	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	60 (66.7)	30 (33.3)	3.3 (1.6, 5.6)	45	28 (62.2)	17 (37.8)	1.5 (0.9, 6.7)	0.7718 (0.4894, 1.2171) 0.2651	0.2646

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.7732
PD	174	91 (52.3)	83 (47.7)	4.4 (2.9, 7.2)	85	44 (51.8)	41 (48.2)	3.2 (1.5, 4.7)	0.7219 (0.5015, 1.0392) 0.0796	0.0780	
PR	48	30 (62.5)	18 (37.5)	4.3 (2.8, 16.4)	22	11 (50.0)	11 (50.0)	5.8 (0.8, NE)	0.9223 (0.4588, 1.8541) 0.8205	0.8052	
SD	82	51 (62.2)	31 (37.8)	4.2 (1.7, 6.7)	55	36 (65.5)	19 (34.5)	2.9 (1.4, 4.5)	0.7301 (0.4738, 1.1249) 0.1538	0.1536	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Reported history of CNS metastases											0.0222
Yes	37	24 (64.9)	13 (35.1)	2.3 (1.4, 5.9)	15	4 (26.7)	11 (73.3)	NE (1.0, NE)	2.1490 (0.7445, 6.2026) 0.1572	0.1440	
No	336	193 (57.4)	143 (42.6)	4.3 (2.9, 6.2)	169	102 (60.4)	67 (39.6)	2.8 (1.5, 4.2)	0.6773 (0.5313, 0.8633) 0.0017	0.0015	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0030
Yes	24	16 (66.7)	8 (33.3)	1.6 (0.9, 5.9)	8	1 (12.5)	7 (87.5)	NE (0.7, NE)	6.1059 (0.8076, 46.1641) 0.0796	0.0430	
No	349	201 (57.6)	148 (42.4)	4.3 (2.9, 5.9)	176	105 (59.7)	71 (40.3)	2.8 (1.5, 3.8)	0.6798 (0.5354, 0.8632) 0.0015	0.0014	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.3335
Normal Function	202	112 (55.4)	90 (44.6)	4.4 (2.9, 7.5)	87	49 (56.3)	38 (43.7)	2.8 (1.5, 4.2)	0.6484 (0.4613, 0.9115) 0.0127	0.0116	
Mild Impairment	123	76 (61.8)	47 (38.2)	4.1 (2.8, 5.7)	69	41 (59.4)	28 (40.6)	2.9 (1.4, 4.7)	0.7965 (0.5419, 1.1708) 0.2470	0.2447	
Moderate Impairment	41	25 (61.0)	16 (39.0)	2.9 (1.6, 16.6)	23	12 (52.2)	11 (47.8)	5.9 (1.4, NE)	1.1270 (0.5652, 2.2473) 0.7342	0.7380	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1473
Normal Function	170	111 (65.3)	59 (34.7)	2.9 (2.8, 4.3)	98	56 (57.1)	42 (42.9)	2.9 (1.5, 5.8)	0.8993 (0.6510, 1.2423) 0.5196	0.5126	
Mild Impairment	195	104 (53.3)	91 (46.7)	5.6 (4.2, 7.5)	84	48 (57.1)	36 (42.9)	2.9 (1.5, 4.2)	0.6043 (0.4264, 0.8564) 0.0046	0.0041	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.8795
Yes	332	190 (57.2)	142 (42.8)	4.2 (2.9, 5.9)	157	90 (57.3)	67 (42.7)	2.9 (1.5, 4.4)	0.7501 (0.5827, 0.9657) 0.0257	0.0252	
No	41	27 (65.9)	14 (34.1)	2.9 (1.5, 7.7)	27	16 (59.3)	11 (40.7)	2.8 (1.5, 5.8)	0.6270 (0.3251, 1.2092) 0.1636	0.1522	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.7289
Positive	331	193 (58.3)	138 (41.7)	4.3 (2.9, 5.9)	163	93 (57.1)	70 (42.9)	2.9 (1.5, 4.3)	0.7249 (0.5646, 0.9307) 0.0116	0.0111	
Negative	42	24 (57.1)	18 (42.9)	2.8 (1.4, 5.9)	21	13 (61.9)	8 (38.1)	3.4 (1.0, 5.9)	0.8914 (0.4528, 1.7546) 0.7393	0.7325	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.2997
Positive	333	194 (58.3)	139 (41.7)	4.3 (2.9, 5.9)	166	97 (58.4)	69 (41.6)	2.8 (1.5, 4.2)	0.7060 (0.5519, 0.9032) 0.0056	0.0053	
Negative	40	23 (57.5)	17 (42.5)	2.8 (1.4, 5.9)	18	9 (50.0)	9 (50.0)	4.5 (1.4, NE)	1.1462 (0.5293, 2.4822) 0.7292	0.7345	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.4897
HER2 IHC 1+	214	105 (49.1)	109 (50.9)	9.9 (7.9, 11.8)	107	45 (42.1)	62 (57.9)	6.3 (4.7, 7.9)	0.7136 (0.4980, 1.0223) 0.0658	0.0638
HER2 IHC 2+/ISH Negative	159	65 (40.9)	94 (59.1)	21.7 (8.5, NE)	77	26 (33.8)	51 (66.2)	7.7 (5.9, NE)	0.9692 (0.6129, 1.5327) 0.8936	0.8860

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.8323
1	221	109 (49.3)	112 (50.7)	10.4 (7.3, 13.1)	100	43 (43.0)	57 (57.0)	6.3 (5.6, 7.9)	0.8402 (0.5870, 1.2027) 0.3415	0.3346
>=2	151	61 (40.4)	90 (59.6)	11.3 (9.7, NE)	83	28 (33.7)	55 (66.3)	7.5 (5.3, NE)	0.7923 (0.5022, 1.2500) 0.3170	0.3151

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.3931
Yes	235	104 (44.3)	131 (55.7)	11.2 (8.3, 17.0)	118	40 (33.9)	78 (66.1)	7.0 (5.7, NE)	0.9296 (0.6425, 1.3450) 0.6984	0.6917	
No	98	48 (49.0)	50 (51.0)	11.1 (7.9, NE)	48	23 (47.9)	25 (52.1)	7.1 (5.6, 11.7)	0.6868 (0.4141, 1.1392) 0.1456	0.1415	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9814
<65	290	132 (45.5)	158 (54.5)	11.1 (9.2, 15.2)	136	51 (37.5)	85 (62.5)	6.9 (5.7, 10.2)	0.8171 (0.5880, 1.1355) 0.2290	0.2247	
>=65	83	38 (45.8)	45 (54.2)	9.9 (5.9, NE)	48	20 (41.7)	28 (58.3)	7.5 (4.4, NE)	0.8301 (0.4792, 1.4380) 0.5066	0.5062	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7537
<75	359	163 (45.4)	196 (54.6)	11.1 (8.5, 15.2)	175	67 (38.3)	108 (61.7)	7.0 (5.7, 10.2)	0.8091 (0.6056, 1.0810) 0.1518	0.1484	
>=75	14	7 (50.0)	7 (50.0)	8.5 (2.1, NE)	9	4 (44.4)	5 (55.6)	NE (0.7, NE)	1.0681 (0.3117, 3.6601) 0.9165	0.8982	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.9928
White	176	81 (46.0)	95 (54.0)	10.3 (7.2, 19.2)	91	34 (37.4)	57 (62.6)	5.9 (5.3, 10.2)	0.8352 (0.5548, 1.2574) 0.3883	0.3827	
Non-White	197	89 (45.2)	108 (54.8)	11.8 (8.3, NE)	92	37 (40.2)	55 (59.8)	7.1 (5.7, 14.8)	0.7964 (0.5396, 1.1756) 0.2519	0.2522	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Region										0.9681
Asia	147	68 (46.3)	79 (53.7)	12.4 (8.3, NE)	66	26 (39.4)	40 (60.6)	7.1 (5.7, NE)	0.8308 (0.5258, 1.3129)	0.4277
North America	60	22 (36.7)	38 (63.3)	19.2 (2.9, NE)	33	10 (30.3)	23 (69.7)	6.3 (4.5, NE)	0.8444 (0.3933, 1.8129)	0.6623
Europe + Israel	166	80 (48.2)	86 (51.8)	10.2 (7.1, 12.7)	85	35 (41.2)	50 (58.8)	6.3 (4.4, 11.7)	0.8253 (0.5504, 1.2375)	0.3470

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
ECOG PS										0.8210
0	200	92 (46.0)	108 (54.0)	11.8 (8.4, 21.7)	105	37 (35.2)	68 (64.8)	7.1 (5.7, 14.8)	0.8533 (0.5795, 1.2566)	0.4171
1	173	78 (45.1)	95 (54.9)	10.4 (7.2, 13.6)	79	34 (43.0)	45 (57.0)	6.9 (4.5, 10.2)	0.7701 (0.5097, 1.1635)	0.2121

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)									0.4998
0	60	29 (48.3)	31 (51.7) (4.1, NE)	34	13 (38.2)	21 (61.8) (3.0, 14.8)	0.8730 (0.4501, 1.6932) 0.6878	0.6884	
1	108	49 (45.4)	59 (54.6) (7.1, 21.7)	51	22 (43.1)	29 (56.9) (5.7, NE)	0.8690 (0.5227, 1.4446) 0.5881	0.5820	
2	115	55 (47.8)	60 (52.2) (7.3, NE)	54	25 (46.3)	29 (53.7) (4.2, 7.9)	0.6046 (0.3699, 0.9883) 0.0448	0.0424	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	No. of subjects censored (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]		
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	37 (41.1)	53 (58.9)	15.2 (9.7, NE)	45	11 (24.4)	34 (75.6)	NE (5.7, NE)	1.1980 (0.6055, 2.3706) 0.6038	0.6003

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.6604
PD	174	78 (44.8)	96 (55.2)	10.3 (7.1, 17.0)	85	31 (36.5)	54 (63.5)	7.0 (5.3, 7.9)	0.8666 (0.5667, 1.3251) 0.5086	0.5016	
PR	48	22 (45.8)	26 (54.2)	12.5 (10.2, NE)	22	8 (36.4)	14 (63.6)	11.7 (3.1, NE)	0.6526 (0.2838, 1.5010) 0.3153	0.3191	
SD	82	32 (39.0)	50 (61.0)	19.2 (8.4, NE)	55	24 (43.6)	31 (56.4)	5.9 (5.7, NE)	0.6402 (0.3734, 1.0977) 0.1050	0.1020	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.5117
Yes	37	16 (43.2)	21 (56.8)	12.5 (7.1, NE)	15	3 (20.0)	12 (80.0)	NE (5.9, NE)	1.0503 (0.2985, 3.6948) 0.9391	0.9391	
No	336	154 (45.8)	182 (54.2)	10.5 (8.4, 13.6)	169	68 (40.2)	101 (59.8)	7.0 (5.7, 10.2)	0.8147 (0.6096, 1.0889) 0.1662	0.1628	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.2931
Yes	24	11 (45.8)	13 (54.2)	9.7 (4.2, NE)	8	2 (25.0)	6 (75.0)	NE (4.7, NE)	1.5246 (0.3343, 6.9527) 0.5860	0.5833	
No	349	159 (45.6)	190 (54.4)	11.1 (8.5, 15.2)	176	69 (39.2)	107 (60.8)	7.0 (5.7, 10.2)	0.7993 (0.5995, 1.0656) 0.1267	0.1239	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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## Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months)	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months)	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Renal function at baseline										0.3332
Normal Function	202	97 (48.0)	105 (52.0)	10.2 (7.5, 13.6)	87	33 (37.9)	54 (62.1)	6.3 (5.3, NE)	0.8235 (0.5503, 1.2323)	0.3409
Mild Impairment	123	51 (41.5)	72 (58.5)	12.5 (8.3, NE)	69	28 (40.6)	41 (59.4)	6.3 (4.7, 10.2)	0.6315 (0.3912, 1.0193)	0.0565
Moderate Impairment	41	21 (51.2)	20 (48.8)	9.9 (3.4, NE)	23	9 (39.1)	14 (60.9)	NE (1.4, NE)	1.2971 (0.5927, 2.8385)	0.5079

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1425
Normal Function	170	79 (46.5)	91 (53.5)	12.5 (8.5, 19.2)	98	45 (45.9)	53 (54.1)	6.9 (5.6, 7.7)	0.6680 (0.4596, 0.9709) 0.0344	0.0323	
Mild Impairment	195	91 (46.7)	104 (53.3)	9.7 (7.1, 13.1)	84	26 (31.0)	58 (69.0)	10.2 (5.3, NE)	1.0508 (0.6756, 1.6343) 0.8260	0.8260	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.3824
Yes	332	148 (44.6)	184 (55.4)	11.1 (9.7, 15.2)	157	57 (36.3)	100 (63.7)	7.5 (6.3, 14.8)	0.8589 (0.6301, 1.1709) 0.3361	0.3317	
No	41	22 (53.7)	19 (46.3)	7.1 (1.6, NE)	27	14 (51.9)	13 (48.1)	5.3 (3.0, 5.9)	0.7414 (0.3718, 1.4783) 0.3954	0.3868	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.5978
Positive	331	151 (45.6)	180 (54.4)	11.1 (8.5, 15.2)	163	62 (38.0)	101 (62.0)	7.1 (5.9, 11.7)	0.8322 (0.6164, 1.1236) 0.2305	0.2262	
Negative	42	19 (45.2)	23 (54.8)	12.5 (3.0, NE)	21	9 (42.9)	12 (57.1)	5.3 (1.4, NE)	0.7562 (0.3341, 1.7112) 0.5024	0.5047	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Hormon receptor status (derived)										0.6176
Positive	333	151 (45.3)	182 (54.7)	11.1 (9.2, 17.0)	166	63 (38.0)	103 (62.0)	7.1 (5.9, 11.7)	0.8277 (0.6140, 1.1159) 0.2148	0.2107
Negative	40	19 (47.5)	21 (52.5)	8.5 (2.9, NE)	18	8 (44.4)	10 (55.6)	5.3 (1.1, NE)	0.7302 (0.3130, 1.7033) 0.4668	0.4694

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.6597
HER2 IHC 1+	214	113 (52.8)	101 (47.2)	5.7 (4.2, 9.7)	107	56 (52.3)	51 (47.7)	4.3 (3.2, 6.9)	0.7492 (0.5410, 1.0376) 0.0822	0.0788	
HER2 IHC 2+/ISH Negative	159	92 (57.9)	67 (42.1)	7.0 (4.4, 8.1)	77	41 (53.2)	36 (46.8)	5.3 (2.8, 8.6)	0.8416 (0.5800, 1.2212) 0.3639	0.3502	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.5114
1	221	127 (57.5)	94 (42.5)	5.0 (3.7, 7.0)	100	57 (57.0)	43 (43.0)	4.2 (2.8, 6.3)	0.8630 (0.6302, 1.1819) 0.3584	0.3473
>=2	151	78 (51.7)	73 (48.3)	8.1 (5.6, 12.5)	83	40 (48.2)	43 (51.8)	5.9 (3.9, 8.5)	0.6607 (0.4449, 0.9811) 0.0399	0.0374

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.7252
Yes	235	127 (54.0)	108 (46.0)	6.2 (4.4, 8.4)	118	63 (53.4)	55 (46.6)	4.2 (2.8, 6.3)	0.7271 (0.5352, 0.9879) 0.0416	0.0382	
No	98	55 (56.1)	43 (43.9)	6.9 (3.5, 14.7)	48	25 (52.1)	23 (47.9)	5.8 (3.5, 11.3)	0.8418 (0.5213, 1.3593) 0.4811	0.4745	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6204
<65	290	164 (56.6)	126 (43.4)	5.9 (4.4, 7.7)	136	71 (52.2)	65 (47.8)	4.4 (3.9, 6.1)	0.7896 (0.5951, 1.0478) 0.1018	0.0950	
>=65	83	41 (49.4)	42 (50.6)	7.0 (3.7, 17.0)	48	26 (54.2)	22 (45.8)	4.2 (1.5, 11.3)	0.6960 (0.4212, 1.1503) 0.1574	0.1561	

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[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6918
<75	359	199 (55.4)	160 (44.6)	5.9 (4.4, 7.7)	175	92 (52.6)	83 (47.4)	4.2 (3.1, 5.9)	0.7648 (0.5950, 0.9832) 0.0364	0.0336	
>=75	14	6 (42.9)	8 (57.1)	14.1 (1.6, NE)	9	5 (55.6)	4 (44.4)	11.1 (0.8, NE)	0.9266 (0.2814, 3.0514) 0.9002	0.9002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.6147
White	176	95 (54.0)	81 (46.0)	6.2 (4.4, 9.9)	91	48 (52.7)	43 (47.3)	3.9 (2.8, 5.8)	0.7115 (0.4992, 1.0142) 0.0598	0.0555	
Non-White	197	110 (55.8)	87 (44.2)	6.5 (4.2, 8.4)	92	49 (53.3)	43 (46.7)	5.8 (4.2, 8.5)	0.8391 (0.5972, 1.1790) 0.3121	0.3051	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.0993
Asia	147	90 (61.2)	57 (38.8)	5.0 (4.1, 7.5)	66	39 (59.1)	27 (40.9)	5.8 (1.7, 8.5)	0.8571 (0.5871, 1.2512) 0.4243	0.4176	
North America	60	28 (46.7)	32 (53.3)	5.6 (1.6, 12.5)	33	8 (24.2)	25 (75.8)	7.9 (4.4, NE)	1.5051 (0.6781, 3.3410) 0.3149	0.3132	
Europe + Israel	166	87 (52.4)	79 (47.6)	7.1 (5.6, 11.8)	85	50 (58.8)	35 (41.2)	3.2 (2.7, 5.7)	0.6036 (0.4222, 0.8628) 0.0056	0.0048	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.8108
0	200	110 (55.0)	90 (45.0)	7.0 (5.0, 11.1)	105	52 (49.5)	53 (50.5)	5.3 (2.8, 7.9)	0.7639 (0.5468, 1.0673) 0.1146	0.1114	
1	173	95 (54.9)	78 (45.1)	5.4 (3.5, 8.1)	79	45 (57.0)	34 (43.0)	4.2 (3.1, 7.0)	0.7931 (0.5528, 1.1378) 0.2080	0.1979	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.7191
0	60	40 (66.7)	20 (33.3)	4.2 (2.2, 5.6)	34	18 (52.9)	16 (47.1)	5.6 (1.5, 9.0)	0.9845 (0.5602, 1.7302)	0.9510 0.9566
1	108	53 (49.1)	55 (50.9)	7.5 (4.2, 13.1)	51	28 (54.9)	23 (45.1)	5.8 (3.0, 11.1)	0.8148 (0.5139, 1.2918)	0.3688 0.3837
2	115	62 (53.9)	53 (46.1)	7.0 (4.4, 12.7)	54	26 (48.1)	28 (51.9)	4.2 (2.8, 8.5)	0.6955 (0.4331, 1.1167)	0.1280 0.1328

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	50 (55.6)	40 (44.4)	6.9 (4.2, 16.0)	45	25 (55.6)	20 (44.4)	4.2 (1.5, 5.8)	0.7081 (0.4343, 1.1545) 0.1664	0.1621	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.1756
PD	174	85 (48.9)	89 (51.1)	7.1 (5.6, 13.9)	85	39 (45.9)	46 (54.1)	5.8 (3.3, 6.9)	0.7374 (0.4999, 1.0878)	0.1246
PR	48	25 (52.1)	23 (47.9)	7.7 (4.2, NE)	22	15 (68.2)	7 (31.8)	3.6 (0.8, 8.6)	0.4990 (0.2606, 0.9555)	0.0360
SD	82	53 (64.6)	29 (35.4)	4.2 (2.4, 7.0)	55	32 (58.2)	23 (41.8)	4.4 (2.3, 9.3)	1.0355 (0.6656, 1.6109)	0.8771

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.4923
Yes	37	20 (54.1)	17 (45.9)	7.2 (3.7, NE)	15	5 (33.3)	10 (66.7)	8.5 (1.4, 12.9)	1.0510 (0.3881, 2.8463) 0.9220	0.9241	
No	336	185 (55.1)	151 (44.9)	6.0 (4.4, 7.7)	169	92 (54.4)	77 (45.6)	4.2 (3.2, 5.9)	0.7690 (0.5968, 0.9909) 0.0423	0.0394	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.2562
Yes	24	15 (62.5)	9 (37.5)	7.2 (1.6, 18.6)	8	3 (37.5)	5 (62.5)	8.5 (1.7, 12.9)	1.3588 (0.3881, 4.7568) 0.6315	0.6300	
No	349	190 (54.4)	159 (45.6)	6.2 (4.4, 7.7)	176	94 (53.4)	82 (46.6)	4.2 (3.2, 5.9)	0.7658 (0.5960, 0.9839) 0.0369	0.0340	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.6020
Normal Function	202	110 (54.5)	92 (45.5)	7.1 (5.3, 10.4)	87	48 (55.2)	39 (44.8)	4.2 (3.0, 5.7)	0.6876 (0.4867, 0.9713) 0.0336	0.0304	
Mild Impairment	123	73 (59.3)	50 (40.7)	4.9 (3.7, 7.2)	69	36 (52.2)	33 (47.8)	4.2 (2.7, 7.9)	0.8257 (0.5502, 1.2391) 0.3551	0.3542	
Moderate Impairment	41	20 (48.8)	21 (51.2)	7.0 (1.6, NE)	23	11 (47.8)	12 (52.2)	11.1 (1.5, NE)	0.9703 (0.4608, 2.0431) 0.9368	0.9324	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.5935
Normal Function	170	98 (57.6)	72 (42.4)	5.6 (4.1, 8.3)	98	54 (55.1)	44 (44.9)	5.8 (3.3, 7.9)	0.8295 (0.5924, 1.1615)	0.2617	
Mild Impairment	195	106 (54.4)	89 (45.6)	7.0 (4.4, 8.8)	84	43 (51.2)	41 (48.8)	3.9 (2.3, 5.7)	0.7084 (0.4936, 1.0168)	0.0597	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.8475
Yes	332	181 (54.5)	151 (45.5)	6.9 (5.0, 8.1)	157	82 (52.2)	75 (47.8)	4.3 (3.1, 6.9)	0.7663 (0.5882, 0.9982) 0.0485	0.0461	
No	41	24 (58.5)	17 (41.5)	4.2 (1.4, NE)	27	15 (55.6)	12 (44.4)	4.4 (1.5, 9.0)	0.9331 (0.4859, 1.7920) 0.8353	0.8174	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.4973
Positive	331	179 (54.1)	152 (45.9)	6.9 (5.0, 9.7)	163	84 (51.5)	79 (48.5)	4.3 (3.2, 7.0)	0.7655 (0.5887, 0.9954) 0.0461	0.0434	
Negative	42	26 (61.9)	16 (38.1)	3.1 (1.8, 7.6)	21	13 (61.9)	8 (38.1)	5.3 (1.5, 6.9)	0.9441 (0.4794, 1.8591) 0.8678	0.8556	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.3960
Positive	333	181 (54.4)	152 (45.6)	6.9 (4.4, 8.4)	166	88 (53.0)	78 (47.0)	4.2 (3.2, 6.3)	0.7596 (0.5867, 0.9835) 0.0370	0.0343	
Negative	40	24 (60.0)	16 (40.0)	4.7 (2.8, 7.7)	18	9 (50.0)	9 (50.0)	5.9 (1.5, 9.0)	0.9927 (0.4566, 2.1584) 0.9853	0.9772	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.4378
HER2 IHC 1+	214	126 (58.9)	88 (41.1)	4.3 (3.0, 8.2)	107	66 (61.7)	41 (38.3)	2.8 (1.5, 4.4)	0.6598 (0.4863, 0.8951) 0.0075	0.0073	
HER2 IHC 2+/ISH Negative	159	85 (53.5)	74 (46.5)	9.7 (4.3, 12.5)	77	41 (53.2)	36 (46.8)	4.4 (3.1, 6.2)	0.7918 (0.5435, 1.1535) 0.2240	0.2168	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.0970
1	221	135 (61.1)	86 (38.9)	4.2 (3.0, 5.9)	100	57 (57.0)	43 (43.0)	4.2 (1.5, 6.0)	0.8542 (0.6254, 1.1667) 0.3218	0.3282	
>=2	151	76 (50.3)	75 (49.7)	10.8 (5.6, 13.6)	83	50 (60.2)	33 (39.8)	3.4 (2.1, 5.4)	0.5532 (0.3823, 0.8003) 0.0017	0.0013	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.7276
Yes	235	132 (56.2)	103 (43.8)	5.6 (4.2, 8.5)	118	70 (59.3)	48 (40.7)	2.8 (1.9, 4.4)	0.6941 (0.5176, 0.9307) 0.0147	0.0140	
No	98	60 (61.2)	38 (38.8)	5.9 (3.5, 12.8)	48	27 (56.3)	21 (43.8)	5.4 (1.5, 7.9)	0.7634 (0.4800, 1.2143) 0.2543	0.2526	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0930
<65	290	162 (55.9)	128 (44.1)	7.0 (4.2, 10.0)	136	80 (58.8)	56 (41.2)	2.8 (1.7, 4.3)	0.6451 (0.4915, 0.8465) 0.0016	0.0014	
>=65	83	49 (59.0)	34 (41.0)	5.6 (3.1, 10.8)	48	27 (56.3)	21 (43.8)	6.5 (3.1, 8.6)	0.9228 (0.5680, 1.4994) 0.7457	0.7369	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0605
<75	359	202 (56.3)	157 (43.7)	5.9 (4.2, 9.7)	175	103 (58.9)	72 (41.1)	3.2 (2.0, 4.4)	0.6748 (0.5300, 0.8591) 0.0014	0.0013	
>=75	14	9 (64.3)	5 (35.7)	6.3 (0.9, 13.3)	9	4 (44.4)	5 (55.6)	11.3 (3.1, NE)	1.9407 (0.5918, 6.3643) 0.2739	0.2654	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.8897
White	176	100 (56.8)	76 (43.2)	4.3 (2.8, 10.0)	91	53 (58.2)	38 (41.8)	3.1 (1.8, 4.4)	0.7311 (0.5213, 1.0255) 0.0697	0.0677	
Non-White	197	111 (56.3)	86 (43.7)	7.0 (4.2, 11.3)	92	54 (58.7)	38 (41.3)	4.4 (1.9, 5.9)	0.6942 (0.4988, 0.9661) 0.0304	0.0286	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.6284
Asia	147	91 (61.9)	56 (38.1)	6.7 (4.2, 11.3)	66	42 (63.6)	24 (36.4)	4.2 (1.5, 6.0)	0.6828 (0.4713, 0.9893) 0.0437	0.0419	
North America	60	28 (46.7)	32 (53.3)	5.8 (2.8, 11.2)	33	19 (57.6)	14 (42.4)	2.1 (1.4, 4.7)	0.5933 (0.3275, 1.0750) 0.0852	0.0809	
Europe + Israel	166	92 (55.4)	74 (44.6)	5.6 (3.1, 10.3)	85	46 (54.1)	39 (45.9)	4.2 (2.7, 6.5)	0.8027 (0.5602, 1.1501) 0.2311	0.2256	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
ECOG PS											
0	200	111 (55.5)	89 (44.5)	8.2 (4.3, 11.1)	105	64 (61.0)	41 (39.0)	2.7 (1.5, 4.2)	0.5583 (0.4080, 0.7639) 0.0003	0.0002	0.0236
1	173	100 (57.8)	73 (42.2)	4.2 (2.8, 9.7)	79	43 (54.4)	36 (45.6)	5.4 (3.4, 6.9)	0.9435 (0.6561, 1.3569) 0.7538	0.7359	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.3401
0	60	35 (58.3)	25 (41.7)	3.4 (1.7, 12.5)	34	20 (58.8)	14 (41.2)	4.2 (1.0, 5.9)	0.7150 (0.4069, 1.2565) 0.2436	0.2410	
1	108	59 (54.6)	49 (45.4)	4.2 (2.9, 12.4)	51	30 (58.8)	21 (41.2)	4.4 (1.5, 7.9)	0.7679 (0.4933, 1.1952) 0.2420	0.2397	
2	115	60 (52.2)	55 (47.8)	7.7 (4.4, 12.7)	54	33 (61.1)	21 (38.9)	2.7 (1.5, 5.4)	0.5282 (0.3401, 0.8203) 0.0045	0.0038	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	57 (63.3)	33 (36.7)	6.7 (4.1, 9.7)	45	24 (53.3)	21 (46.7)	4.2 (1.8, 6.2)	0.9223 (0.5683, 1.4969) 0.7435	0.7379

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.3033
PD	174	90 (51.7)	84 (48.3)	5.9 (3.1, 10.8)	85	45 (52.9)	40 (47.1)	4.3 (2.8, 5.8)	0.7719 (0.5341, 1.1156) 0.1682	0.1590	
PR	48	34 (70.8)	14 (29.2)	4.2 (2.8, 7.6)	22	11 (50.0)	11 (50.0)	2.4 (1.0, NE)	0.9186 (0.4620, 1.8264) 0.8087	0.8122	
SD	82	43 (52.4)	39 (47.6)	9.7 (4.3, 21.7)	55	37 (67.3)	18 (32.7)	3.8 (1.4, 6.0)	0.5273 (0.3367, 0.8261) 0.0052	0.0048	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.0979
Yes	37	23 (62.2)	14 (37.8)	3.0 (1.4, 18.1)	15	5 (33.3)	10 (66.7)	6.0 (0.9, NE)	1.5214 (0.5742, 4.0310) 0.3986	0.4054	
No	336	188 (56.0)	148 (44.0)	6.7 (4.2, 9.7)	169	102 (60.4)	67 (39.6)	3.5 (2.1, 4.6)	0.6653 (0.5206, 0.8503) 0.0011	0.0010	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.0208
Yes	24	16 (66.7)	8 (33.3)	3.0 (0.8, 18.1)	8	2 (25.0)	6 (75.0)	NE (0.8, NE)	2.6839 (0.6113, 11.7840) 0.1909	0.1746
No	349	195 (55.9)	154 (44.1)	5.9 (4.2, 9.7)	176	105 (59.7)	71 (40.3)	3.4 (2.1, 4.4)	0.6655 (0.5228, 0.8473) 0.0009	0.0008

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0970
Normal Function	202	115 (56.9)	87 (43.1)	5.6 (3.9, 10.0)	87	52 (59.8)	35 (40.2)	3.4 (1.5, 4.4)	0.6576 (0.4717, 0.9168) 0.0134	0.0125	
Mild Impairment	123	70 (56.9)	53 (43.1)	7.0 (3.4, 12.4)	69	41 (59.4)	28 (40.6)	2.8 (1.5, 4.4)	0.6031 (0.4042, 0.9001) 0.0133	0.0123	
Moderate Impairment	41	24 (58.5)	17 (41.5)	5.6 (1.6, 13.6)	23	11 (47.8)	12 (52.2)	8.6 (5.9, NE)	1.4021 (0.6836, 2.8757) 0.3565	0.3561	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.5918
Normal Function	170	97 (57.1)	73 (42.9)	5.6 (3.5, 12.4)	98	55 (56.1)	43 (43.9)	4.4 (2.3, 6.0)	0.7782 (0.5567, 1.0877)	0.1379	
Mild Impairment	195	113 (57.9)	82 (42.1)	5.9 (4.2, 9.1)	84	51 (60.7)	33 (39.3)	2.9 (1.7, 4.3)	0.6478 (0.4620, 0.9084)	0.0112	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.2900
Yes	332	187 (56.3)	145 (43.7)	5.9 (4.2, 9.7)	157	88 (56.1)	69 (43.9)	4.2 (2.8, 5.4)	0.7422 (0.5742, 0.9593) 0.0228	0.0221	
No	41	24 (58.5)	17 (41.5)	5.6 (1.4, NE)	27	19 (70.4)	8 (29.6)	1.5 (1.0, 4.6)	0.6079 (0.3257, 1.1348) 0.1181	0.1104	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.7891
Positive	331	189 (57.1)	142 (42.9)	5.9 (4.2, 9.7)	163	93 (57.1)	70 (42.9)	4.2 (2.3, 5.4)	0.7188 (0.5588, 0.9246) 0.0102	0.0098	
Negative	42	22 (52.4)	20 (47.6)	5.6 (1.4, NE)	21	14 (66.7)	7 (33.3)	3.4 (1.4, 5.9)	0.6953 (0.3481, 1.3889) 0.3033	0.2922	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.9836
Positive	333	191 (57.4)	142 (42.6)	5.9 (4.2, 9.7)	166	97 (58.4)	69 (41.6)	3.8 (2.1, 4.7)	0.7127 (0.5562, 0.9132) 0.0074	0.0070	
Negative	40	20 (50.0)	20 (50.0)	7.0 (1.6, NE)	18	10 (55.6)	8 (44.4)	4.2 (1.5, 7.0)	0.7162 (0.3276, 1.5658) 0.4030	0.3941	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.4834
HER2 IHC 1+	214	99 (46.3)	115 (53.7)	11.2 (6.2, 21.4)	107	48 (44.9)	59 (55.1)	4.4 (2.8, 11.4)	0.7387 (0.5201, 1.0492) 0.0907	0.0883
HER2 IHC 2+/ISH Negative	159	77 (48.4)	82 (51.6)	10.4 (5.8, 13.9)	77	32 (41.6)	45 (58.4)	7.5 (3.9, NE)	0.8648 (0.5705, 1.3107) 0.4935	0.4905

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.8451
1	221	107 (48.4)	114 (51.6)	10.4 (5.7, 18.3)	100	44 (44.0)	56 (56.0)	11.3 (2.8, 14.0)	0.8112 (0.5686, 1.1573) 0.2484	0.2488
>=2	151	68 (45.0)	83 (55.0)	11.2 (8.1, 21.4)	83	36 (43.4)	47 (56.6)	5.9 (3.8, NE)	0.7237 (0.4797, 1.0917) 0.1231	0.1202

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Prior CDK4/6										0.5669
Yes	235	116 (49.4)	119 (50.6)	8.5 (5.8, 11.8)	118	50 (42.4)	68 (57.6)	4.3 (3.0, NE)	0.8272 (0.5904, 1.1591)	0.2689
No	98	45 (45.9)	53 (54.1)	13.4 (5.9, NE)	48	24 (50.0)	24 (50.0)	8.4 (2.1, 14.0)	0.6818 (0.4148, 1.1206)	0.1291

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2037
<65	290	128 (44.1)	162 (55.9)	13.4 (8.5, 22.3)	136	57 (41.9)	79 (58.1)	4.9 (3.7, NE)	0.7230 (0.5261, 0.9937) 0.0456	0.0431	
>=65	83	48 (57.8)	35 (42.2)	5.8 (4.2, 10.0)	48	23 (47.9)	25 (52.1)	8.4 (2.8, NE)	1.0545 (0.6398, 1.7379) 0.8352	0.8334	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Age											
<75	359	167 (46.5)	192 (53.5)	11.2 (7.8, 17.6)	175	77 (44.0)	98 (56.0)	4.9 (3.7, 11.4)	0.7329 (0.5570, 0.9642) 0.0264	0.0254	0.0360
>=75	14	9 (64.3)	5 (35.7)	5.6 (1.6, NE)	9	3 (33.3)	6 (66.7)	NE (2.8, NE)	2.8254 (0.7617, 10.4795) 0.1204	0.1047	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Race										0.1349
White	176	86 (48.9)	90 (51.1)	8.3 (4.4, 17.6)	91	34 (37.4)	57 (62.6)	5.3 (3.0, NE)	0.9960 (0.6669, 1.4874) 0.9844	0.9829
Non-White	197	90 (45.7)	107 (54.3)	13.1 (7.8, 22.8)	92	46 (50.0)	46 (50.0)	5.9 (3.3, 11.3)	0.6261 (0.4362, 0.8989) 0.0112	0.0104

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Region										0.3232
Asia	147	72 (49.0)	75 (51.0)	11.8 (7.2, 22.8)	66	35 (53.0)	31 (47.0)	4.7 (2.1, 11.3)	0.6070 (0.4025, 0.9155) 0.0173	0.0161
North America	60	24 (40.0)	36 (60.0)	8.5 (4.2, NE)	33	9 (27.3)	24 (72.7)	NE (2.7, NE)	1.0586 (0.4868, 2.3019) 0.8858	0.8880
Europe + Israel	166	80 (48.2)	86 (51.8)	8.6 (4.5, 17.6)	85	36 (42.4)	49 (57.6)	7.5 (3.4, NE)	0.9107 (0.6121, 1.3549) 0.6444	0.6424

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	200	100 (50.0)	100 (50.0)	10.0 (7.2, 13.9)	105	47 (44.8)	58 (55.2)	4.4 (2.8, 14.0)	0.7279 (0.5121, 1.0347) 0.0768	0.0754	0.5101
1	173	76 (43.9)	97 (56.1)	11.4 (5.8, 18.3)	79	33 (41.8)	46 (58.2)	7.5 (4.0, NE)	0.8621 (0.5696, 1.3050) 0.4831	0.4749	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.9912
0	60	25 (41.7)	35 (58.3)	13.9 (5.2, NE)	34	12 (35.3)	22 (64.7)	5.9 (1.7, NE)	0.7974 (0.3941, 1.6133) 0.5289	0.5289	
1	108	49 (45.4)	59 (54.6)	11.5 (5.0, NE)	51	25 (49.0)	26 (51.0)	6.1 (2.3, 14.0)	0.7695 (0.4743, 1.2486) 0.2887	0.2921	
2	115	53 (46.1)	62 (53.9)	11.2 (5.6, NE)	54	21 (38.9)	33 (61.1)	7.5 (2.8, NE)	0.8875 (0.5311, 1.4833) 0.6489	0.6418	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	49 (54.4)	41 (45.6)	8.6 (5.7, 13.4)	45	22 (48.9)	23 (51.1)	4.2 (2.1, NE)	0.7275 (0.4344, 1.2184) 0.2266	0.2205

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.5522
PD	174	72 (41.4)	102 (58.6)	11.8 (7.8, NE)	85	38 (44.7)	47 (55.3)	4.4 (2.7, 11.4)	0.6263 (0.4196, 0.9348) 0.0220	0.0210
PR	48	22 (45.8)	26 (54.2)	13.9 (5.7, NE)	22	10 (45.5)	12 (54.5)	4.3 (1.7, NE)	0.6197 (0.2886, 1.3305) 0.2196	0.2170
SD	82	44 (53.7)	38 (46.3)	6.7 (4.4, 18.3)	55	26 (47.3)	29 (52.7)	8.4 (2.8, NE)	0.8881 (0.5432, 1.4522) 0.6363	0.6369

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.6838
Yes	37	16 (43.2)	21 (56.8)	11.2 (4.2, NE)	15	4 (26.7)	11 (73.3)	NE (1.0, NE)	1.0191 (0.3368, 3.0838) 0.9732	0.9697
No	336	160 (47.6)	176 (52.4)	10.6 (7.1, 13.9)	169	76 (45.0)	93 (55.0)	5.3 (3.9, 11.3)	0.7727 (0.5857, 1.0193) 0.0681	0.0661

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.1588
Yes	24	10 (41.7)	14 (58.3)	NE (4.9, NE)	8	1 (12.5)	7 (87.5)	NE (1.4, NE)	2.6115 (0.3302, 20.6556)	0.3405
No	349	166 (47.6)	183 (52.4)	10.4 (7.1, 13.9)	176	79 (44.9)	97 (55.1)	4.9 (3.8, 11.3)	0.7605 (0.5796, 0.9978)	0.0467

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Renal function at baseline										0.0780
Normal Function	202	90 (44.6)	112 (55.4)	11.2 (7.8, 25.0)	87	40 (46.0)	47 (54.0)	4.3 (3.3, 8.4)	0.6275 (0.4285, 0.9189)	0.0166
Mild Impairment	123	63 (51.2)	60 (48.8)	8.1 (5.6, 13.9)	69	29 (42.0)	40 (58.0)	6.1 (2.3, NE)	0.8778 (0.5603, 1.3750)	0.5646
Moderate Impairment	41	20 (48.8)	21 (51.2)	11.2 (4.2, NE)	23	7 (30.4)	16 (69.6)	NE (11.3, NE)	1.6748 (0.7075, 3.9649)	0.2313

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.2822
Normal Function	170	82 (48.2)	88 (51.8)	11.8 (7.1, 22.3)	98	46 (46.9)	52 (53.1)	6.1 (2.8, 11.4)	0.7128 (0.4938, 1.0289) 0.0707	0.0683
Mild Impairment	195	92 (47.2)	103 (52.8)	8.6 (6.2, 13.9)	84	32 (38.1)	52 (61.9)	5.3 (3.9, NE)	0.8959 (0.5961, 1.3465) 0.5969	0.5955

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline visceral disease										0.4002
Yes	332	160 (48.2)	172 (51.8)	10.0 (7.1, 13.1)	157	68 (43.3)	89 (56.7)	6.1 (3.7, 11.4)	0.8038 (0.6032, 1.0709)	0.1352 (0.1357)
No	41	16 (39.0)	25 (61.0)	25.0 (2.9, NE)	27	12 (44.4)	15 (55.6)	5.3 (1.7, 14.0)	0.6538 (0.3031, 1.4104)	0.2721 (0.2787)

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (IXRS)										0.9604
Positive	331	159 (48.0)	172 (52.0)	10.4 (7.1, 13.4)	163	71 (43.6)	92 (56.4)	6.1 (3.7, 11.4)	0.7831 (0.5900, 1.0394) 0.0905	0.0899
Negative	42	17 (40.5)	25 (59.5)	13.9 (4.2, NE)	21	9 (42.9)	12 (57.1)	5.9 (3.4, NE)	0.8070 (0.3502, 1.8597) 0.6146	0.6086

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (derived)										0.6161
Positive	333	160 (48.0)	173 (52.0)	10.4 (7.1, 13.4)	166	74 (44.6)	92 (55.4)	4.9 (3.7, 11.4)	0.7651 (0.5788, 1.0114) 0.0601	0.0592
Negative	40	16 (40.0)	24 (60.0)	13.9 (2.9, NE)	18	6 (33.3)	12 (66.7)	NE (1.7, NE)	1.0107 (0.3855, 2.6496) 0.9828	0.9882

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0456
HER2 IHC 1+	214	156 (72.9)	58 (27.1)	1.4 (1.4, 1.7)	107	38 (35.5)	69 (64.5)	8.6 (6.0, NE)	2.6228 (1.8362, 3.7466) <0.0001	<0.0001	
HER2 IHC 2+/ISH Negative	159	102 (64.2)	57 (35.8)	1.6 (1.4, 2.8)	77	35 (45.5)	42 (54.5)	6.7 (4.6, 13.3)	1.5382 (1.0462, 2.2615) 0.0285	0.0290	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.9838
1	221	154 (69.7)	67 (30.3)	1.4 (1.4, 1.8)	100	42 (42.0)	58 (58.0)	7.0 (5.9, 11.3)	2.0363 (1.4444, 2.8707) <0.0001	<0.0001	
>=2	151	103 (68.2)	48 (31.8)	1.6 (1.4, 2.9)	83	31 (37.3)	52 (62.7)	8.6 (5.4, NE)	2.0619 (1.3777, 3.0860) 0.0004	0.0004	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Prior CDK4/6										0.7770
Yes	235	164 (69.8)	71 (30.2)	1.6 (1.4, 2.4)	118	45 (38.1)	73 (61.9)	6.7 (5.4, 13.3)	2.1248 (1.5259, 2.9587)	<0.0001
No	98	69 (70.4)	29 (29.6)	1.4 (0.9, 2.8)	48	22 (45.8)	26 (54.2)	8.6 (4.2, 14.8)	1.8209 (1.1233, 2.9515)	0.0152

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6782
<65	290	204 (70.3)	86 (29.7)	1.4 (1.4, 1.8)	136	52 (38.2)	84 (61.8)	8.6 (5.9, 13.3)	2.1338 (1.5716, 2.8970) <0.0001	<0.0001	
>=65	83	54 (65.1)	29 (34.9)	1.6 (1.4, 2.8)	48	21 (43.8)	27 (56.3)	7.5 (4.6, NE)	1.8782 (1.1294, 3.1236) 0.0152	0.0141	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3547
<75	359	247 (68.8)	112 (31.2)	1.5 (1.4, 1.8)	175	69 (39.4)	106 (60.6)	7.5 (5.9, 9.8)	2.0140 (1.5403, 2.6334) <0.0001	<0.0001	
>=75	14	11 (78.6)	3 (21.4)	1.4 (0.9, 2.8)	9	4 (44.4)	5 (55.6)	11.3 (0.7, NE)	5.3742 (1.4186, 20.3597) 0.0133	0.0069	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.3873
White	176	126 (71.6)	50 (28.4)	1.4 (1.4, 1.6)	91	33 (36.3)	58 (63.7)	8.2 (5.1, NE)	2.3899 (1.6265, 3.5115) <0.0001	<0.0001	
Non-White	197	132 (67.0)	65 (33.0)	1.6 (1.4, 2.8)	92	40 (43.5)	52 (56.5)	8.6 (5.9, 11.3)	1.8005 (1.2611, 2.5707) 0.0012	0.0011	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.4643
Asia	147	100 (68.0)	47 (32.0)	1.7 (1.4, 3.0)	66	30 (45.5)	36 (54.5)	8.6 (4.7, 14.8)	1.6366 (1.0856, 2.4674) 0.0187	0.0186	
North America	60	40 (66.7)	20 (33.3)	1.4 (0.9, 2.4)	33	9 (27.3)	24 (72.7)	6.3 (5.9, 13.3)	2.5724 (1.2440, 5.3194) 0.0108	0.0084	
Europe + Israel	166	118 (71.1)	48 (28.9)	1.4 (1.4, 1.6)	85	34 (40.0)	51 (60.0)	7.0 (4.6, 9.8)	2.4090 (1.6409, 3.5366) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											
0	200	139 (69.5)	61 (30.5)	1.4 (1.4, 2.4)	105	41 (39.0)	64 (61.0)	7.0 (5.1, 14.8)	1.9519 (1.3751, 2.7707) 0.0002	0.0001	0.5676
1	173	119 (68.8)	54 (31.2)	1.5 (1.4, 2.1)	79	32 (40.5)	47 (59.5)	8.6 (5.9, 13.3)	2.2256 (1.5033, 3.2949) 0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.9264
0	60	39 (65.0)	21 (35.0)	1.4 (1.0, 2.9)	34	11 (32.4)	23 (67.6)	9.0 (5.9, 14.8)	2.1593 (1.1027, 4.2285) 0.0248	0.0213	
1	108	67 (62.0)	41 (38.0)	1.8 (1.4, 2.9)	51	20 (39.2)	31 (60.8)	9.0 (4.7, NE)	2.0310 (1.2298, 3.3542) 0.0056	0.0047	
2	115	84 (73.0)	31 (27.0)	1.5 (1.4, 2.8)	54	21 (38.9)	33 (61.1)	6.3 (4.6, NE)	2.3686 (1.4658, 3.8274) 0.0004	0.0003	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	68 (75.6)	22 (24.4)	1.4 (1.0, 1.7)	45	21 (46.7)	24 (53.3)	5.6 (1.5, NE)	1.8551 (1.1339, 3.0350) 0.0139	0.0138

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.8851
PD	174	113 (64.9)	61 (35.1)	1.5 (1.4, 2.8)	85	32 (37.6)	53 (62.4)	7.0 (5.1, 9.8)	2.0291 (1.3682, 3.0092) 0.0004	0.0003	
PR	48	36 (75.0)	12 (25.0)	1.4 (0.9, 1.6)	22	9 (40.9)	13 (59.1)	8.6 (1.7, NE)	2.4341 (1.1673, 5.0757) 0.0177	0.0154	
SD	82	57 (69.5)	25 (30.5)	1.6 (1.4, 3.2)	55	23 (41.8)	32 (58.2)	9.0 (4.7, 14.8)	1.8542 (1.1385, 3.0197) 0.0131	0.0120	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.7574
Yes	37	26 (70.3)	11 (29.7)	1.4 (0.9, 2.9)	15	4 (26.7)	11 (73.3)	NE (1.0, NE)	2.5730 (0.8970, 7.3811) 0.0788	0.0672	
No	336	232 (69.0)	104 (31.0)	1.5 (1.4, 1.8)	169	69 (40.8)	100 (59.2)	8.2 (5.9, 9.8)	2.0380 (1.5554, 2.6702) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.6107
Yes	24	16 (66.7)	8 (33.3)	1.4 (0.9, 13.0)	8	2 (25.0)	6 (75.0)	NE (0.8, NE)	2.8754 (0.6549, 12.6247) 0.1617	0.1407	
No	349	242 (69.3)	107 (30.7)	1.5 (1.4, 1.8)	176	71 (40.3)	105 (59.7)	8.2 (5.9, 9.8)	2.0485 (1.5704, 2.6723) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.9363
Normal Function	202	140 (69.3)	62 (30.7)	1.6 (1.4, 2.8)	87	34 (39.1)	53 (60.9)	8.6 (5.1, 14.8)	1.9768 (1.3570, 2.8797) 0.0004	0.0003	
Mild Impairment	123	89 (72.4)	34 (27.6)	1.4 (1.4, 1.6)	69	28 (40.6)	41 (59.4)	7.5 (4.2, 9.8)	2.1841 (1.4234, 3.3512) 0.0003	0.0003	
Moderate Impairment	41	26 (63.4)	15 (36.6)	2.1 (1.0, 4.2)	23	10 (43.5)	13 (56.5)	8.2 (5.9, NE)	2.0099 (0.9627, 4.1961) 0.0631	0.0586	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Hepatic function at baseline										0.5304
Normal Function	170	133 (78.2)	37 (21.8)	1.4 (1.0, 1.4)	98	44 (44.9)	54 (55.1)	7.5 (5.4, 9.0)	2.2349 (1.5854, 3.1504) <0.0001	<0.0001
Mild Impairment	195	122 (62.6)	73 (37.4)	2.2 (1.5, 2.9)	84	29 (34.5)	55 (65.5)	9.8 (5.1, 13.3)	1.9638 (1.3082, 2.9480) 0.0011	0.0009

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]	
Baseline visceral disease										0.4064	
Yes	332	227 (68.4)	105 (31.6)	1.5 (1.4, 2.2)	157	58 (36.9)	99 (63.1)	8.6 (6.3, 13.3)	2.2026 (1.6487, 2.9427)	<0.0001	
No	41	31 (75.6)	10 (24.4)	1.4 (0.9, 1.8)	27	15 (55.6)	12 (44.4)	5.9 (1.2, 9.0)	1.6103 (0.8622, 3.0073)	0.1372	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Hormon receptor status (IXRS)											
Positive	331	232 (70.1)	99 (29.9)	1.5 (1.4, 1.8)	163	65 (39.9)	98 (60.1)	8.2 (5.9, 11.3)	2.0891 (1.5846, 2.7543) <0.0001	<0.0001	0.8140
Negative	42	26 (61.9)	16 (38.1)	1.6 (1.0, 4.2)	21	8 (38.1)	13 (61.9)	9.0 (1.0, NE)	1.8598 (0.8372, 4.1315) 0.1276	0.1185	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.4896
Positive	333	231 (69.4)	102 (30.6)	1.5 (1.4, 2.1)	166	67 (40.4)	99 (59.6)	7.5 (5.9, 9.8)	2.0053 (1.5258, 2.6354) <0.0001	<0.0001	
Negative	40	27 (67.5)	13 (32.5)	1.4 (0.9, 2.8)	18	6 (33.3)	12 (66.7)	9.0 (1.5, NE)	2.7259 (1.1147, 6.6664) 0.0280	0.0227	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.8668
HER2 IHC 1+	214	113 (52.8)	101 (47.2)	9.6 (4.6, 11.8)	107	57 (53.3)	50 (46.7)	3.4 (2.1, 7.0)	0.5947 (0.4284, 0.8254) 0.0019	0.0017	
HER2 IHC 2+/ISH Negative	159	75 (47.2)	84 (52.8)	9.2 (6.9, 13.3)	77	40 (51.9)	37 (48.1)	4.7 (2.7, 7.2)	0.6404 (0.4336, 0.9459) 0.0251	0.0236	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.7777
1	221	118 (53.4)	103 (46.6)	8.5 (4.7, 11.1)	100	58 (58.0)	42 (42.0)	2.8 (1.5, 5.8)	0.5884 (0.4269, 0.8109) 0.0012	0.0010
>=2	151	69 (45.7)	82 (54.3)	10.6 (7.3, 27.2)	83	39 (47.0)	44 (53.0)	5.9 (3.4, 9.3)	0.6339 (0.4232, 0.9493) 0.0269	0.0253

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.3009
Yes	235	118 (50.2)	117 (49.8)	8.3 (4.6, 11.2)	118	60 (50.8)	58 (49.2)	4.4 (2.7, 7.3)	0.6654 (0.4850, 0.9128) 0.0116	0.0108	
No	98	54 (55.1)	44 (44.9)	9.7 (7.4, 13.4)	48	29 (60.4)	19 (39.6)	2.8 (1.4, 7.0)	0.5045 (0.3175, 0.8017) 0.0038	0.0032	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											0.1237
<65	290	141 (48.6)	149 (51.4)	9.7 (7.7, 13.1)	136	72 (52.9)	64 (47.1)	4.0 (2.3, 5.8)	0.5588 (0.4181, 0.7469) 0.0001	<0.0001	
>=65	83	47 (56.6)	36 (43.4)	5.6 (2.8, 11.2)	48	25 (52.1)	23 (47.9)	7.0 (1.5, 8.3)	0.8560 (0.5204, 1.4081) 0.5403	0.5449	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7286
<75	359	183 (51.0)	176 (49.0)	9.2 (7.1, 11.1)	175	93 (53.1)	82 (46.9)	4.4 (2.4, 5.9)	0.6036 (0.4676, 0.7791) 0.0001	<0.0001	
>=75	14	5 (35.7)	9 (64.3)	NE (0.9, NE)	9	4 (44.4)	5 (55.6)	NE (0.7, NE)	0.9748 (0.2612, 3.6388) 0.9697	0.9698	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.8538
White	176	82 (46.6)	94 (53.4)	8.7 (5.8, 14.1)	91	44 (48.4)	47 (51.6)	4.0 (2.7, 7.7)	0.6134 (0.4226, 0.8903) 0.0101	0.0093	
Non-White	197	106 (53.8)	91 (46.2)	9.2 (5.4, 11.2)	92	52 (56.5)	40 (43.5)	4.6 (1.8, 6.1)	0.6330 (0.4506, 0.8892) 0.0084	0.0077	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.8691
Asia	147	84 (57.1)	63 (42.9)	9.6 (5.4, 12.7)	66	40 (60.6)	26 (39.4)	4.2 (1.5, 5.9)	0.5908 (0.4017, 0.8690) 0.0075	0.0067	
North America	60	22 (36.7)	38 (63.3)	10.6 (2.9, NE)	33	14 (42.4)	19 (57.6)	4.5 (1.5, 7.2)	0.6086 (0.3065, 1.2088) 0.1561	0.1471	
Europe + Israel	166	82 (49.4)	84 (50.6)	8.7 (5.7, 12.6)	85	43 (50.6)	42 (49.4)	4.4 (2.7, 7.7)	0.6599 (0.4537, 0.9598) 0.0297	0.0279	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.4115
0	200	110 (55.0)	90 (45.0)	8.7 (5.7, 11.8)	105	58 (55.2)	47 (44.8)	3.0 (1.5, 5.8)	0.5555 (0.4012, 0.7690) 0.0004	0.0003	
1	173	78 (45.1)	95 (54.9)	9.7 (5.9, 13.3)	79	39 (49.4)	40 (50.6)	5.8 (3.2, 9.8)	0.7126 (0.4814, 1.0546) 0.0902	0.0860	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.4163
0	60	31 (51.7)	29 (48.3)	7.7 (4.2, 17.6)	34	17 (50.0)	17 (50.0)	5.4 (1.4, 9.8)	0.6267 (0.3418, 1.1489)	0.1271
1	108	53 (49.1)	55 (50.9)	8.8 (5.6, 13.5)	51	24 (47.1)	27 (52.9)	8.3 (3.1, 14.1)	0.8343 (0.5138, 1.3547)	0.4624
2	115	57 (49.6)	58 (50.4)	10.5 (4.2, 13.3)	54	27 (50.0)	27 (50.0)	4.4 (2.1, 7.5)	0.6304 (0.3916, 1.0147)	0.0527

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Pain

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	47 (52.2)	43 (47.8)	10.2 (4.3, 13.4)	45	29 (64.4)	16 (35.6)	2.0 (1.4, 4.6)	0.4621 (0.2842, 0.7513) 0.0019	0.0014

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Pain

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.7522
PD	174	80 (46.0)	94 (54.0)	9.6 (5.6, 12.7)	85	41 (48.2)	44 (51.8)	5.8 (2.7, 7.7)	0.6424 (0.4373, 0.9436) 0.0241	0.0229
PR	48	26 (54.2)	22 (45.8)	9.7 (4.2, 16.4)	22	9 (40.9)	13 (59.1)	7.0 (1.6, NE)	0.7993 (0.3662, 1.7445) 0.5737	0.5518
SD	82	46 (56.1)	36 (43.9)	9.7 (4.3, 14.1)	55	33 (60.0)	22 (40.0)	4.0 (1.5, 9.3)	0.5759 (0.3625, 0.9147) 0.0194	0.0187

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Reported history of CNS metastases											0.2940
Yes	37	17 (45.9)	20 (54.1)	8.5 (5.4, NE)	15	4 (26.7)	11 (73.3)	NE (1.5, NE)	1.0651 (0.3523, 3.2206) 0.9110	0.9063	
No	336	171 (50.9)	165 (49.1)	9.6 (6.9, 11.2)	169	93 (55.0)	76 (45.0)	4.4 (2.4, 5.8)	0.6000 (0.4633, 0.7771) 0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.1595
Yes	24	11 (45.8)	13 (54.2)	9.6 (5.4, NE)	8	2 (25.0)	6 (75.0)	NE (0.8, NE)	1.3891 (0.3033, 6.3614) 0.6721	0.6679	
No	349	177 (50.7)	172 (49.3)	9.2 (7.0, 11.2)	176	95 (54.0)	81 (46.0)	4.4 (2.4, 5.8)	0.5975 (0.4629, 0.7713) 0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Renal function at baseline											0.2410
Normal Function	202	98 (48.5)	104 (51.5)	10.2 (8.3, 12.7)	87	47 (54.0)	40 (46.0)	4.0 (2.0, 7.2)	0.5070 (0.3539, 0.7263) 0.0002	0.0002	
Mild Impairment	123	66 (53.7)	57 (46.3)	5.8 (3.0, 13.1)	69	36 (52.2)	33 (47.8)	4.4 (1.5, 7.0)	0.7147 (0.4722, 1.0818) 0.1123	0.1086	
Moderate Impairment	41	21 (51.2)	20 (48.8)	8.8 (4.2, 13.5)	23	11 (47.8)	12 (52.2)	7.3 (3.1, NE)	0.9779 (0.4699, 2.0351) 0.9523	0.9596	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.5553
Normal Function	170	95 (55.9)	75 (44.1)	8.5 (4.4, 11.1)	98	53 (54.1)	45 (45.9)	4.4 (2.7, 5.8)	0.7105 (0.5051, 0.9994) 0.0496	0.0463	
Mild Impairment	195	91 (46.7)	104 (53.3)	10.2 (7.1, 13.1)	84	42 (50.0)	42 (50.0)	7.2 (2.0, 8.7)	0.5689 (0.3908, 0.8282) 0.0032	0.0029	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.4947
Yes	332	164 (49.4)	168 (50.6)	9.7 (7.1, 12.5)	157	83 (52.9)	74 (47.1)	4.2 (2.4, 7.0)	0.6054 (0.4624, 0.7925) 0.0003	0.0002	
No	41	24 (58.5)	17 (41.5)	7.7 (2.8, 12.6)	27	14 (51.9)	13 (48.1)	4.4 (1.5, 9.8)	0.7297 (0.3688, 1.4438) 0.3654	0.3557	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.9664
Positive	331	172 (52.0)	159 (48.0)	8.8 (7.0, 10.6)	163	87 (53.4)	76 (46.6)	4.2 (2.4, 6.1)	0.6103 (0.4691, 0.7939) 0.0002	0.0002	
Negative	42	16 (38.1)	26 (61.9)	17.6 (4.7, NE)	21	10 (47.6)	11 (52.4)	5.9 (1.4, NE)	0.7317 (0.3269, 1.6376) 0.4472	0.4383	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.5850
Positive	333	171 (51.4)	162 (48.6)	8.8 (7.1, 10.6)	166	89 (53.6)	77 (46.4)	4.2 (2.4, 6.1)	0.5991 (0.4613, 0.7782) 0.0001	0.0001	
Negative	40	17 (42.5)	23 (57.5)	17.6 (1.6, NE)	18	8 (44.4)	10 (55.6)	5.9 (1.4, NE)	0.9099 (0.3875, 2.1365) 0.8284	0.8198	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0926
HER2 IHC 1+	214	98 (45.8)	116 (54.2)	11.2 (7.1, 15.7)	107	37 (34.6)	70 (65.4)	NE (5.0, NE)	0.9281 (0.6329, 1.3610) 0.7025	0.7073	
HER2 IHC 2+/ISH Negative	159	66 (41.5)	93 (58.5)	21.7 (8.1, NE)	77	37 (48.1)	40 (51.9)	6.5 (3.8, 9.4)	0.5811 (0.3847, 0.8779) 0.0099	0.0089	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.6882
1	221	102 (46.2)	119 (53.8)	11.3 (6.9, 20.9)	100	42 (42.0)	58 (58.0)	6.5 (4.5, NE)	0.8097 (0.5624, 1.1660)	0.2555
>=2	151	62 (41.1)	89 (58.9)	15.3 (8.3, NE)	83	32 (38.6)	51 (61.4)	7.5 (4.4, NE)	0.6692 (0.4330, 1.0341)	0.0688

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.7119
Yes	235	104 (44.3)	131 (55.7)	11.8 (8.1, 16.7)	118	45 (38.1)	73 (61.9)	6.7 (4.4, NE)	0.7797 (0.5448, 1.1158)	0.1719	
No	98	45 (45.9)	53 (54.1)	12.5 (5.9, 27.2)	48	21 (43.8)	27 (56.3)	7.5 (3.8, NE)	0.7235 (0.4293, 1.2192)	0.2240	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6233
<65	290	128 (44.1)	162 (55.9)	12.5 (8.3, 20.9)	136	51 (37.5)	85 (62.5)	6.5 (5.1, NE)	0.7781 (0.5583, 1.0845) 0.1386	0.1368	
>=65	83	36 (43.4)	47 (56.6)	11.1 (5.6, NE)	48	23 (47.9)	25 (52.1)	6.7 (1.7, NE)	0.6958 (0.4114, 1.1767) 0.1761	0.1755	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1676
<75	359	156 (43.5)	203 (56.5)	12.5 (8.8, 21.7)	175	69 (39.4)	106 (60.6)	6.5 (5.0, NE)	0.7264 (0.5440, 0.9698) 0.0301	0.0296	
>=75	14	8 (57.1)	6 (42.9)	5.6 (0.9, NE)	9	5 (55.6)	4 (44.4)	13.7 (1.4, NE)	1.7052 (0.5499, 5.2878) 0.3554	0.3477	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.8034
White	176	70 (39.8)	106 (60.2)	15.7 (10.2, NE)	91	33 (36.3)	58 (63.7)	6.8 (4.5, NE)	0.7151 (0.4677, 1.0934) 0.1217	0.1197	
Non-White	197	94 (47.7)	103 (52.3)	9.3 (6.9, 27.2)	92	41 (44.6)	51 (55.4)	6.1 (4.4, NE)	0.7783 (0.5372, 1.1275) 0.1851	0.1856	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.1704
Asia	147	73 (49.7)	74 (50.3)	9.3 (6.5, 27.2)	66	29 (43.9)	37 (56.1)	6.5 (4.7, NE)	0.8603 (0.5574, 1.3277) 0.4967	0.4977	
North America	60	22 (36.7)	38 (63.3)	13.2 (4.5, NE)	33	16 (48.5)	17 (51.5)	3.1 (1.4, 5.0)	0.4012 (0.2029, 0.7936) 0.0087	0.0071	
Europe + Israel	166	69 (41.6)	97 (58.4)	16.7 (8.8, NE)	85	29 (34.1)	56 (65.9)	7.5 (6.5, NE)	0.8495 (0.5457, 1.3225) 0.4701	0.4683	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.3791
0	200	95 (47.5)	105 (52.5)	11.2 (7.5, 21.7)	105	39 (37.1)	66 (62.9)	6.7 (5.1, NE)	0.8403 (0.5749, 1.2283) 0.3690	0.3711	
1	173	69 (39.9)	104 (60.1)	15.3 (7.1, NE)	79	35 (44.3)	44 (55.7)	6.8 (3.8, NE)	0.6612 (0.4376, 0.9989) 0.0494	0.0473	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.3229
0	60	23 (38.3)	37 (61.7)	11.1 (5.8, NE)	34	14 (41.2)	20 (58.8)	5.8 (2.9, NE)	0.5632 (0.2861, 1.1085) 0.0965	0.0942	
1	108	47 (43.5)	61 (56.5)	15.7 (5.6, 24.1)	51	17 (33.3)	34 (66.7)	NE (4.2, NE)	1.0302 (0.5854, 1.8130) 0.9179	0.9192	
2	115	59 (51.3)	56 (48.7)	8.1 (5.7, 13.2)	54	24 (44.4)	30 (55.6)	6.7 (2.1, 9.7)	0.7680 (0.4726, 1.2480) 0.2866	0.2823	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	35 (38.9)	55 (61.1)	NE (6.9, NE)	45	19 (42.2)	26 (57.8)	8.4 (1.6, NE)	0.5896 (0.3339, 1.0411) 0.0686	0.0664

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.6858
PD	174	72 (41.4)	102 (58.6)	15.3 (5.8, 27.2)	85	31 (36.5)	54 (63.5)	7.5 (5.1, NE)	0.8529 (0.5570, 1.3059) 0.4640	0.4633	
PR	48	19 (39.6)	29 (60.4)	NE (10.2, NE)	22	9 (40.9)	13 (59.1)	6.7 (1.7, NE)	0.6235 (0.2757, 1.4102) 0.2566	0.2529	
SD	82	32 (39.0)	50 (61.0)	NE (7.9, NE)	55	24 (43.6)	31 (56.4)	6.8 (3.1, NE)	0.6174 (0.3607, 1.0567) 0.0786	0.0755	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.3541
Yes	37	13 (35.1)	24 (64.9)	NE (4.5, NE)	15	5 (33.3)	10 (66.7)	NE (0.8, NE)	0.5289 (0.1833, 1.5263) 0.2388	0.2332
No	336	151 (44.9)	185 (55.1)	11.8 (8.1, 16.7)	169	69 (40.8)	100 (59.2)	6.7 (5.1, 13.7)	0.7785 (0.5827, 1.0400) 0.0902	0.0894

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.5392
Yes	24	9 (37.5)	15 (62.5)	NE (4.4, NE)	8	3 (37.5)	5 (62.5)	NE (0.7, NE)	0.6218 (0.1625, 2.3797) 0.4878	0.4928	
No	349	155 (44.4)	194 (55.6)	11.8 (8.3, 20.9)	176	71 (40.3)	105 (59.7)	6.7 (5.1, 13.7)	0.7623 (0.5729, 1.0143) 0.0625	0.0617	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.8662
Normal Function	202	80 (39.6)	122 (60.4)	16.7 (10.2, NE)	87	30 (34.5)	57 (65.5)	8.4 (4.4, NE)	0.7708 (0.5028, 1.1817) 0.2324	0.2295	
Mild Impairment	123	62 (50.4)	61 (49.6)	8.3 (5.6, 13.2)	69	27 (39.1)	42 (60.9)	6.5 (5.0, NE)	0.8395 (0.5279, 1.3348) 0.4596	0.4600	
Moderate Impairment	41	19 (46.3)	22 (53.7)	9.1 (4.2, NE)	23	13 (56.5)	10 (43.5)	5.9 (1.5, NE)	0.7589 (0.3745, 1.5379) 0.4439	0.4410	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.5447
Normal Function	170	80 (47.1)	90 (52.9)	11.1 (7.1, NE)	98	43 (43.9)	55 (56.1)	6.7 (4.5, 13.7)	0.7311 (0.5023, 1.0642) 0.1021	0.1009
Mild Impairment	195	82 (42.1)	113 (57.9)	13.2 (7.1, 21.7)	84	29 (34.5)	55 (65.5)	9.7 (4.2, NE)	0.8476 (0.5508, 1.3043) 0.4521	0.4503

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.6952
Yes	332	145 (43.7)	187 (56.3)	12.5 (8.8, 20.9)	157	63 (40.1)	94 (59.9)	6.8 (5.0, NE)	0.7267 (0.5377, 0.9820) 0.0377	0.0373	
No	41	19 (46.3)	22 (53.7)	5.8 (3.1, NE)	27	11 (40.7)	16 (59.3)	6.7 (4.4, NE)	1.0000 (0.4749, 2.1057) 1.0000	0.9975	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.7712
Positive	331	146 (44.1)	185 (55.9)	12.5 (8.3, 20.9)	163	65 (39.9)	98 (60.1)	6.7 (5.0, NE)	0.7410 (0.5505, 0.9974) 0.0480	0.0476	
Negative	42	18 (42.9)	24 (57.1)	9.3 (3.3, NE)	21	9 (42.9)	12 (57.1)	5.9 (2.9, NE)	0.8882 (0.3930, 2.0076) 0.7758	0.7716	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.6841
Positive	333	149 (44.7)	184 (55.3)	12.5 (8.3, 20.9)	166	66 (39.8)	100 (60.2)	6.7 (5.0, NE)	0.7659 (0.5705, 1.0283) 0.0760	0.0754	
Negative	40	15 (37.5)	25 (62.5)	11.1 (4.6, NE)	18	8 (44.4)	10 (55.6)	5.9 (1.5, NE)	0.6588 (0.2739, 1.5843) 0.3512	0.3429	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
HER2 status										0.2878
HER2 IHC 1+	214	92 (43.0)	122 (57.0)	12.0 (7.8, 18.6)	107	47 (43.9)	60 (56.1)	5.8 (2.9, 10.2)	0.5967 (0.4153, 0.8572)	0.0047
HER2 IHC 2+/ISH Negative	159	57 (35.8)	102 (64.2)	18.3 (11.1, NE)	77	38 (49.4)	39 (50.6)	5.3 (3.7, 10.0)	0.4178 (0.2738, 0.6375)	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.3206
1	221	92 (41.6)	129 (58.4)	12.0 (8.3, NE)	100	46 (46.0)	54 (54.0)	5.4 (3.3, 12.0)	0.5892 (0.4108, 0.8451) 0.0040	0.0037
>=2	151	56 (37.1)	95 (62.9)	16.6 (11.1, NE)	83	39 (47.0)	44 (53.0)	5.3 (2.8, 7.0)	0.4097 (0.2665, 0.6297) <0.0001	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Prior CDK4/6										0.7806
Yes	235	89 (37.9)	146 (62.1)	16.1 (9.7, NE)	118	51 (43.2)	67 (56.8)	5.0 (3.2, 10.2)	0.5353 (0.3765, 0.7612) 0.0005	0.0004
No	98	44 (44.9)	54 (55.1)	16.0 (9.6, NE)	48	26 (54.2)	22 (45.8)	5.4 (2.9, 7.0)	0.4407 (0.2654, 0.7316) 0.0015	0.0011

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Age											
<65	290	113 (39.0)	177 (61.0)	17.6 (10.1, NE)	136	64 (47.1)	72 (52.9)	5.0 (3.7, 6.1)	0.4592 (0.3345, 0.6303)	<0.0001	0.1702
>=65	83	36 (43.4)	47 (56.6)	11.8 (7.1, 18.6)	48	21 (43.8)	27 (56.3)	6.5 (2.8, NE)	0.6909 (0.3960, 1.2054)	0.1893	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Age										0.0309
<75	359	140 (39.0)	219 (61.0)	16.1 (11.1, NE)	175	81 (46.3)	94 (53.7)	5.0 (3.8, 7.0)	0.4751 (0.3578, 0.6310)	<0.0001
>=75	14	9 (64.3)	5 (35.7)	4.2 (1.4, NE)	9	4 (44.4)	5 (55.6)	NE (0.7, NE)	1.7710 (0.5381, 5.8289)	0.3439

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Race										0.6442
White	176	74 (42.0)	102 (58.0)	11.1 (8.3, 18.3)	91	41 (45.1)	50 (54.9)	5.3 (2.8, 10.0)	0.5329 (0.3589, 0.7912) 0.0018	0.0015
Non-White	197	75 (38.1)	122 (61.9)	16.6 (11.7, NE)	92	44 (47.8)	48 (52.2)	5.4 (3.7, 12.0)	0.4892 (0.3338, 0.7170) 0.0002	0.0002

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Region										0.7389
Asia	147	59 (40.1)	88 (59.9)	NE (11.7, NE)	66	35 (53.0)	31 (47.0)	5.0 (2.9, 12.0)	0.4891 (0.3188, 0.7503) 0.0011	0.0008
North America	60	19 (31.7)	41 (68.3)	NE (4.4, NE)	33	10 (30.3)	23 (69.7)	NE (1.8, NE)	0.7441 (0.3442, 1.6086) 0.4523	0.4542
Europe + Israel	166	71 (42.8)	95 (57.2)	11.2 (8.3, 17.6)	85	40 (47.1)	45 (52.9)	5.9 (2.8, 10.0)	0.4752 (0.3165, 0.7134) 0.0003	0.0002

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	200	77 (38.5)	123 (61.5)	16.1 (11.1, NE)	105	52 (49.5)	53 (50.5)	5.3 (1.8, 6.5)	0.3814 (0.2649, 0.5492)	<0.0001	0.0210
1	173	72 (41.6)	101 (58.4)	16.0 (7.3, 18.3)	79	33 (41.8)	46 (58.2)	6.1 (4.2, NE)	0.7578 (0.4973, 1.1549)	0.1919	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.8997
0	60	30 (50.0)	30 (50.0)	9.2 (5.9, 17.6)	34	17 (50.0)	17 (50.0)	5.3 (1.7, 5.9)	0.5302 (0.2857, 0.9838) 0.0442	0.0405	
1	108	37 (34.3)	71 (65.7)	NE (9.3, NE)	51	24 (47.1)	27 (52.9)	6.5 (1.5, 10.2)	0.5279 (0.3141, 0.8871) 0.0159	0.0142	
2	115	46 (40.0)	69 (60.0)	NE (7.3, NE)	54	23 (42.6)	31 (57.4)	4.5 (2.1, NE)	0.5721 (0.3422, 0.9565) 0.0332	0.0309	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.3.5.2 - EORTC QLQ-C30 - First deterioration - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	36 (40.0)	54 (60.0)	16.0 (11.2, NE)	45	21 (46.7)	24 (53.3)	4.2 (1.9, NE)	0.4086 (0.2302, 0.7254) 0.0022	0.0017	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.3450
PD	174	63 (36.2)	111 (63.8)	16.6 (9.6, NE)	85	37 (43.5)	48 (56.5)	4.7 (2.8, NE)	0.4621 (0.3034, 0.7040) 0.0003	0.0002
PR	48	18 (37.5)	30 (62.5)	16.1 (11.7, NE)	22	12 (54.5)	10 (45.5)	4.2 (1.0, 7.0)	0.3122 (0.1437, 0.6779) 0.0033	0.0018
SD	82	36 (43.9)	46 (56.1)	17.6 (8.7, NE)	55	27 (49.1)	28 (50.9)	6.1 (2.9, 10.2)	0.5806 (0.3450, 0.9773) 0.0407	0.0386

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.5417
Yes	37	16 (43.2)	21 (56.8)	11.1 (5.6, NE)	15	5 (33.3)	10 (66.7)	2.8 (0.9, NE)	0.6629 (0.2371, 1.8533) 0.4332	0.4424	
No	336	133 (39.6)	203 (60.4)	16.1 (11.1, NE)	169	80 (47.3)	89 (52.7)	5.4 (4.2, 7.0)	0.4987 (0.3744, 0.6643) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.3807
Yes	24	8 (33.3)	16 (66.7)	NE (8.3, NE)	8	2 (25.0)	6 (75.0)	NE (1.4, NE)	0.8469 (0.1753, 4.0917) 0.8361	0.8416	
No	349	141 (40.4)	208 (59.6)	16.0 (10.1, 18.6)	176	83 (47.2)	93 (52.8)	5.3 (3.8, 6.5)	0.5042 (0.3810, 0.6671) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Renal function at baseline										0.2293
Normal Function	202	78 (38.6)	124 (61.4)	16.0 (10.6, NE)	87	42 (48.3)	45 (51.7)	4.3 (2.8, 5.9)	0.4192 (0.2835, 0.6200)	<0.0001
Mild Impairment	123	51 (41.5)	72 (58.5)	13.4 (9.0, NE)	69	30 (43.5)	39 (56.5)	6.1 (2.8, 10.2)	0.5537 (0.3454, 0.8878)	0.0126
Moderate Impairment	41	18 (43.9)	23 (56.1)	9.3 (4.3, NE)	23	10 (43.5)	13 (56.5)	NE (1.9, NE)	0.9517 (0.4382, 2.0669)	0.9040

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.8385
Normal Function	170	78 (45.9)	92 (54.1)	11.8 (8.7, 18.3)	98	49 (50.0)	49 (50.0)	5.0 (2.9, 6.1)	0.5255 (0.3635, 0.7597) 0.0006	0.0005
Mild Impairment	195	70 (35.9)	125 (64.1)	17.6 (11.1, NE)	84	34 (40.5)	50 (59.5)	7.1 (3.2, NE)	0.5416 (0.3554, 0.8254) 0.0043	0.0041

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.2308
Yes	332	131 (39.5)	201 (60.5)	16.0 (11.1, 18.6)	157	69 (43.9)	88 (56.1)	5.9 (4.2, 10.0)	0.5488 (0.4069, 0.7403) 0.0001	<0.0001	
No	41	18 (43.9)	23 (56.1)	11.7 (6.3, NE)	27	16 (59.3)	11 (40.7)	4.5 (1.2, 5.8)	0.3391 (0.1635, 0.7034) 0.0037	0.0025	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.8677
Positive	331	133 (40.2)	198 (59.8)	16.0 (10.6, NE)	163	74 (45.4)	89 (54.6)	5.8 (4.2, 7.1)	0.5153 (0.3847, 0.6904)	<0.0001	
Negative	42	16 (38.1)	26 (61.9)	17.6 (3.1, NE)	21	11 (52.4)	10 (47.6)	4.7 (1.4, NE)	0.5395 (0.2438, 1.1938)	0.1175	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.4827
Positive	333	131 (39.3)	202 (60.7)	16.0 (11.1, NE)	166	77 (46.4)	89 (53.6)	5.4 (3.8, 7.1)	0.4974 (0.3723, 0.6646) <0.0001	<0.0001	
Negative	40	18 (45.0)	22 (55.0)	10.6 (4.3, NE)	18	8 (44.4)	10 (55.6)	5.3 (1.4, NE)	0.6967 (0.2940, 1.6510) 0.4116	0.4064	

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[c] Two-sided p-value from unstratified log-rank test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
HER2 status										0.7755
HER2 IHC 1+	214	123 (57.5)	91 (42.5)	5.1 (2.9, 8.1)	107	46 (43.0)	61 (57.0)	6.5 (4.0, 11.3)	1.1361 (0.8068, 1.5999)	0.4811
HER2 IHC 2+/ISH Negative	159	92 (57.9)	67 (42.1)	5.5 (2.9, 8.5)	77	34 (44.2)	43 (55.8)	6.3 (5.0, 14.4)	1.2142 (0.8187, 1.8007)	0.3413

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.1026
1	221	134 (60.6)	87 (39.4)	4.2 (2.8, 5.7)	100	42 (42.0)	58 (58.0)	8.5 (4.6, NE)	1.4447 (1.0206, 2.0449) 0.0380	0.0386
>=2	151	81 (53.6)	70 (46.4)	7.4 (4.3, 11.8)	83	38 (45.8)	45 (54.2)	6.1 (3.8, 9.8)	0.8827 (0.5965, 1.3061) 0.5325	0.5200

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6									0.3656
Yes	235	135 (57.4)	100 (42.6) (2.9, 7.7)	118	47 (39.8)	71 (60.2) (4.4, NE)	1.2504 (0.8951, 1.7467) 0.1901	0.1948	
No	98	58 (59.2)	40 (40.8) (3.1, 11.2)	48	26 (54.2)	22 (45.8) (3.1, 11.3)	0.9589 (0.6027, 1.5255) 0.8593	0.8529	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Age										0.7723
<65	290	165 (56.9)	125 (43.1)	5.1 (3.2, 8.1)	136	56 (41.2)	80 (58.8)	6.2 (4.4, 9.8)	1.1771 (0.8676, 1.5970)	0.3032
>=65	83	50 (60.2)	33 (39.8)	5.6 (1.6, 8.5)	48	24 (50.0)	24 (50.0)	7.0 (4.2, 11.7)	1.2182 (0.7466, 1.9876)	0.4376

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4244
<75	359	203 (56.5)	156 (43.5)	5.6 (4.2, 7.7)	175	73 (41.7)	102 (58.3)	7.0 (5.1, 9.8)	1.1724 (0.8956, 1.5346) 0.2470	0.2576	
>=75	14	12 (85.7)	2 (14.3)	2.1 (1.4, 4.2)	9	7 (77.8)	2 (22.2)	6.5 (0.7, 14.4)	2.4946 (0.9164, 6.7907) 0.0736	0.0659	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.4947
White	176	96 (54.5)	80 (45.5)	5.6 (2.9, 8.6)	91	38 (41.8)	53 (58.2)	5.1 (4.0, 9.0)	1.0710 (0.7324, 1.5661) 0.7234	0.7325	
Non-White	197	119 (60.4)	78 (39.6)	4.7 (2.9, 7.6)	92	42 (45.7)	50 (54.3)	8.5 (4.4, 11.7)	1.2453 (0.8745, 1.7732) 0.2238	0.2308	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.5841
Asia	147	97 (66.0)	50 (34.0)	4.2 (2.8, 7.4)	66	31 (47.0)	35 (53.0)	8.5 (3.8, 14.4)	1.3526 (0.9015, 2.0295) 0.1446	0.1454	
North America	60	27 (45.0)	33 (55.0)	5.6 (1.5, NE)	33	9 (27.3)	24 (72.7)	6.3 (1.5, NE)	1.3091 (0.6097, 2.8108) 0.4896	0.4920	
Europe + Israel	166	91 (54.8)	75 (45.2)	6.1 (2.9, 10.6)	85	40 (47.1)	45 (52.9)	6.2 (4.2, 9.0)	1.0000 (0.6862, 1.4573) 1.0000	0.9846	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.3660
0	200	114 (57.0)	86 (43.0)	7.0 (4.2, 11.2)	105	45 (42.9)	60 (57.1)	7.0 (4.1, 11.7)	1.0507 (0.7425, 1.4868) 0.7801	0.7926	
1	173	101 (58.4)	72 (41.6)	4.2 (2.3, 5.9)	79	35 (44.3)	44 (55.7)	6.3 (5.0, 11.3)	1.3619 (0.9251, 2.0049) 0.1175	0.1215	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.6765
0	60	31 (51.7)	29 (48.3)	5.6 (1.4, NE)	34	14 (41.2)	20 (58.8)	5.9 (1.3, NE)	1.0401 (0.5510, 1.9634) 0.9034	0.9204
1	108	61 (56.5)	47 (43.5)	5.5 (2.3, 10.6)	51	22 (43.1)	29 (56.9)	8.5 (6.1, NE)	1.3579 (0.8321, 2.2159) 0.2207	0.2219
2	115	64 (55.7)	51 (44.3)	7.0 (4.2, 11.2)	54	24 (44.4)	30 (55.6)	5.1 (3.9, 11.7)	0.9239 (0.5716, 1.4932) 0.7465	0.7317

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	59 (65.6)	31 (34.4)	4.2 (1.6, 7.7)	45	20 (44.4)	25 (55.6)	6.2 (2.1, NE)	1.3450 (0.8080, 2.2390) 0.2543	0.2562	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.6603
PD	174	94 (54.0)	80 (46.0)	6.9 (3.2, 10.2)	85	38 (44.7)	47 (55.3)	6.3 (3.4, 8.5)	0.9580 (0.6544, 1.4023) 0.8252	0.8145
PR	48	32 (66.7)	16 (33.3)	2.8 (0.9, 6.2)	22	10 (45.5)	12 (54.5)	6.0 (1.4, NE)	1.3510 (0.6624, 2.7556) 0.4080	0.4308
SD	82	46 (56.1)	36 (43.9)	5.6 (3.9, 12.0)	55	24 (43.6)	31 (56.4)	9.0 (4.2, NE)	1.2527 (0.7638, 2.0546) 0.3721	0.3765

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.9261
Yes	37	19 (51.4)	18 (48.6)	4.5 (1.5, NE)	15	4 (26.7)	11 (73.3)	NE (0.8, NE)	1.4097 (0.4784, 4.1543) 0.5334	0.5320	
No	336	196 (58.3)	140 (41.7)	5.5 (3.4, 7.2)	169	76 (45.0)	93 (55.0)	6.5 (5.0, 9.8)	1.1730 (0.8987, 1.5311) 0.2404	0.2499	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Baseline CNS metastases										0.1896
Yes	24	17 (70.8)	7 (29.2)	1.6 (0.9, 8.5)	8	2 (25.0)	6 (75.0) (0.8, NE)	2.9730 (0.6853, 12.8973) 0.1456	0.1260	
No	349	198 (56.7)	151 (43.3)	5.6 (4.2, 7.7)	176	78 (44.3)	98 (55.7) (5.0, 9.8)	1.1154 (0.8569, 1.4520) 0.4168	0.4317	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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## Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Renal function at baseline											0.1574
Normal Function	202	115 (56.9)	87 (43.1)	5.6 (2.9, 8.5)	87	36 (41.4)	51 (58.6)	6.3 (3.2, NE)	1.1773 (0.8082, 1.7148) 0.3951	0.4072	
Mild Impairment	123	69 (56.1)	54 (43.9)	5.6 (2.8, 11.2)	69	32 (46.4)	37 (53.6)	6.0 (3.4, 9.8)	0.9813 (0.6398, 1.5051) 0.9310	0.9146	
Moderate Impairment	41	28 (68.3)	13 (31.7)	4.2 (1.5, 8.5)	23	9 (39.1)	14 (60.9)	11.3 (6.5, NE)	2.2992 (1.0799, 4.8954) 0.0308	0.0267	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.2170
Normal Function	170	115 (67.6)	55 (32.4)	2.9 (1.6, 5.6)	98	45 (45.9)	53 (54.1)	6.5 (4.0, 11.7)	1.4217 (1.0060, 2.0091) 0.0461	0.0481	
Mild Impairment	195	97 (49.7)	98 (50.3)	8.5 (4.3, 13.5)	84	33 (39.3)	51 (60.7)	6.2 (4.4, 11.3)	1.0115 (0.6784, 1.5082) 0.9551	0.9634	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Baseline visceral disease										0.7098
Yes	332	189 (56.9)	143 (43.1)	5.6 (4.2, 8.1)	157	66 (42.0)	91 (58.0)	7.0 (5.0, 11.3)	1.1946 (0.9010, 1.5838) 0.2166	0.2269
No	41	26 (63.4)	15 (36.6)	2.8 (1.3, 5.1)	27	14 (51.9)	13 (48.1)	5.9 (0.9, NE)	1.1286 (0.5885, 2.1641) 0.7158	0.7158

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (IXRS)										0.8217
Positive	331	192 (58.0)	139 (42.0)	5.6 (3.9, 7.4)	163	71 (43.6)	92 (56.4)	7.0 (4.6, 10.5)	1.1556 (0.8789, 1.5195) 0.3004	0.3102
Negative	42	23 (54.8)	19 (45.2)	2.9 (1.0, 13.5)	21	9 (42.9)	12 (57.1)	6.0 (1.0, NE)	1.3445 (0.6168, 2.9306) 0.4565	0.4580

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]	
Hormon receptor status (derived)										0.6709	
Positive	333	193 (58.0)	140 (42.0)	5.5 (3.9, 7.2)	166	73 (44.0)	93 (56.0)	7.0 (4.6, 10.5)	1.1482 (0.8758, 1.5052)	0.3271	0.3172
Negative	40	22 (55.0)	18 (45.0)	2.9 (0.9, 13.5)	18	7 (38.9)	11 (61.1)	6.0 (1.6, NE)	1.4167 (0.5965, 3.3647)	0.4392	0.4299

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
HER2 status										0.4060
HER2 IHC 1+	214	121 (56.5)	93 (43.5)	4.2 (2.9, 8.2)	107	47 (43.9)	60 (56.1)	5.8 (3.2, 11.3)	1.0267 (0.7299, 1.4443)	0.8861
HER2 IHC 2+/ISH Negative	159	98 (61.6)	61 (38.4)	4.2 (2.8, 5.7)	77	35 (45.5)	42 (54.5)	5.9 (3.2, NE)	1.2508 (0.8490, 1.8428)	0.2634

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.7023
1	221	135 (61.1)	86 (38.9)	3.5 (2.9, 5.7)	100	49 (49.0)	51 (51.0)	4.9 (2.9, 11.2)	1.0548 (0.7589, 1.4662) 0.7507	0.7551
>=2	151	83 (55.0)	68 (45.0)	4.8 (2.8, 10.0)	83	33 (39.8)	50 (60.2)	6.0 (4.4, NE)	1.1919 (0.7928, 1.7920) 0.3988	0.4057

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.3818
Yes	235	139 (59.1)	96 (40.9)	4.3 (2.9, 5.7)	118	50 (42.4)	68 (57.6)	4.9 (3.2, NE)	1.1385 (0.8222, 1.5767) 0.4348	0.4446	
No	98	55 (56.1)	43 (43.9)	5.6 (2.9, 14.5)	48	25 (52.1)	23 (47.9)	6.1 (2.9, 11.2)	0.8751 (0.5422, 1.4124) 0.5850	0.5834	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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[c] Two-sided p-value from unstratified log-rank test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9926
<65	290	171 (59.0)	119 (41.0)	4.2 (2.9, 5.7)	136	58 (42.6)	78 (57.4)	5.6 (3.2, 11.2)	1.1419 (0.8457, 1.5419) 0.3863	0.4007	
>=65	83	48 (57.8)	35 (42.2)	4.4 (2.9, 8.5)	48	24 (50.0)	24 (50.0)	6.7 (2.8, 11.3)	1.1071 (0.6748, 1.8165) 0.6871	0.6832	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5128
<75	359	211 (58.8)	148 (41.2)	4.2 (2.9, 5.6)	175	77 (44.0)	98 (56.0)	5.8 (3.8, 8.4)	1.0984 (0.8442, 1.4293) 0.4847	0.4942	
>=75	14	8 (57.1)	6 (42.9)	5.8 (1.4, NE)	9	5 (55.6)	4 (44.4)	6.7 (1.5, NE)	2.1215 (0.6315, 7.1268) 0.2238	0.2135	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.4094
White	176	98 (55.7)	78 (44.3)	4.3 (2.8, 6.2)	91	40 (44.0)	51 (56.0)	4.7 (3.1, 6.7)	1.0089 (0.6958, 1.4629) 0.9626	0.9641	
Non-White	197	121 (61.4)	76 (38.6)	4.2 (2.9, 7.1)	92	42 (45.7)	50 (54.3)	7.5 (3.3, 11.3)	1.1921 (0.8365, 1.6988) 0.3309	0.3389	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.1852
Asia	147	94 (63.9)	53 (36.1)	4.2 (2.8, 7.1)	66	30 (45.5)	36 (54.5)	8.3 (3.0, 11.3)	1.2581 (0.8318, 1.9029) 0.2767	0.2810	
North America	60	34 (56.7)	26 (43.3)	3.0 (1.5, 9.7)	33	10 (30.3)	23 (69.7)	NE (1.9, NE)	1.6077 (0.7859, 3.2888) 0.1935	0.1884	
Europe + Israel	166	91 (54.8)	75 (45.2)	4.3 (2.8, 8.5)	85	42 (49.4)	43 (50.6)	4.7 (2.8, 6.7)	0.8922 (0.6164, 1.2912) 0.5452	0.5423	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.7656
0	200	120 (60.0)	80 (40.0)	4.3 (2.9, 7.1)	105	44 (41.9)	61 (58.1)	4.9 (3.2, NE)	1.1001 (0.7765, 1.5584) 0.5915	0.5868	
1	173	99 (57.2)	74 (42.8)	4.2 (2.8, 8.3)	79	38 (48.1)	41 (51.9)	5.9 (3.3, 11.3)	1.1468 (0.7864, 1.6723) 0.4766	0.4931	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1594
0	60	37 (61.7)	23 (38.3)	1.7 (1.4, 5.6)	34	13 (38.2)	21 (61.8)	6.0 (2.9, NE)	1.6224 (0.8573, 3.0704) 0.1370	0.1332	
1	108	54 (50.0)	54 (50.0)	7.1 (2.9, 11.1)	51	29 (56.9)	22 (43.1)	3.3 (1.4, 6.1)	0.7298 (0.4639, 1.1481) 0.1730	0.1694	
2	115	75 (65.2)	40 (34.8)	4.3 (2.8, 5.7)	54	23 (42.6)	31 (57.4)	6.7 (2.8, NE)	1.1839 (0.7375, 1.9004) 0.4846	0.4897	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	53 (58.9)	37 (41.1)	4.3 (2.8, 8.5)	45	17 (37.8)	28 (62.2)	8.3 (3.2, NE)	1.3540 (0.7809, 2.3478) 0.2804	0.2831	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.4422
PD	174	94 (54.0)	80 (46.0)	4.3 (2.9, 8.2)	85	32 (37.6)	53 (62.4)	7.5 (3.2, NE)	1.2342 (0.8243, 1.8479) 0.3070	0.3072
PR	48	29 (60.4)	19 (39.6)	8.5 (2.9, 16.7)	22	12 (54.5)	10 (45.5)	4.9 (1.4, 8.4)	0.6590 (0.3293, 1.3188) 0.2388	0.2311
SD	82	52 (63.4)	30 (36.6)	4.2 (2.8, 5.8)	55	27 (49.1)	28 (50.9)	5.9 (3.1, 11.3)	1.2013 (0.7523, 1.9183) 0.4424	0.4523

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.0982
Yes	37	22 (59.5)	15 (40.5)	2.9 (1.5, 12.5)	15	3 (20.0)	12 (80.0)	NE (0.9, NE)	2.7304 (0.8169, 9.1260) 0.1028	0.0884	
No	336	197 (58.6)	139 (41.4)	4.3 (3.0, 5.7)	169	79 (46.7)	90 (53.3)	5.8 (3.3, 8.3)	1.0511 (0.8075, 1.3682) 0.7111	0.7231	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.6756
Yes	24	14 (58.3)	10 (41.7)	4.2 (1.5, 12.5)	8	3 (37.5)	5 (62.5)	5.9 (0.7, NE)	1.3850 (0.3973, 4.8286) 0.6092	0.6122	
No	349	205 (58.7)	144 (41.3)	4.2 (2.9, 5.6)	176	79 (44.9)	97 (55.1)	5.8 (4.4, 8.4)	1.1054 (0.8506, 1.4365) 0.4535	0.4642	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Renal function at baseline										0.2622
Normal Function	202	124 (61.4)	78 (38.6)	4.2 (2.9, 5.6)	87	42 (48.3)	45 (51.7)	3.8 (1.9, 11.2)	0.9577 (0.6729, 1.3630) 0.8103	0.7921
Mild Impairment	123	69 (56.1)	54 (43.9)	3.4 (1.7, 8.6)	69	31 (44.9)	38 (55.1)	5.8 (3.1, 8.3)	1.1129 (0.7251, 1.7082) 0.6246	0.6385
Moderate Impairment	41	25 (61.0)	16 (39.0)	5.8 (3.0, 15.2)	23	8 (34.8)	15 (65.2)	11.3 (4.5, NE)	1.8244 (0.8174, 4.0717) 0.1422	0.1342

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.7465
Normal Function	170	107 (62.9)	63 (37.1)	4.2 (2.9, 5.8)	98	48 (49.0)	50 (51.0)	5.9 (3.2, 8.3)	1.0646 (0.7544, 1.5024) 0.7217	0.7371	
Mild Impairment	195	111 (56.9)	84 (43.1)	3.5 (2.8, 8.5)	84	34 (40.5)	50 (59.5)	5.6 (2.9, NE)	1.1919 (0.8099, 1.7541) 0.3733	0.3761	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.5454
Yes	332	196 (59.0)	136 (41.0)	4.2 (2.9, 5.6)	157	68 (43.3)	89 (56.7)	5.9 (3.3, 11.3)	1.1574 (0.8768, 1.5279) 0.3020	0.3056	
No	41	23 (56.1)	18 (43.9)	5.1 (2.8, 16.7)	27	14 (51.9)	13 (48.1)	5.8 (1.6, 11.2)	0.8167 (0.4087, 1.6323) 0.5666	0.5534	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)									0.5576
Positive	331	195 (58.9)	136 (41.1) (3.0, 5.7)	163	72 (44.2)	91 (55.8) (3.3, 11.2)	1.0889 (0.8293, 1.4298) 0.5398	0.5469	
Negative	42	24 (57.1)	18 (42.9) (1.4, 16.7)	21	10 (47.6)	11 (52.4) (1.5, NE)	1.3654 (0.6451, 2.8902) 0.4156	0.4248	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.1283
Positive	333	193 (58.0)	140 (42.0)	4.4 (3.1, 6.2)	166	75 (45.2)	91 (54.8)	5.8 (3.3, 8.4)	1.0420 (0.7962, 1.3636) 0.7644	0.7716	
Negative	40	26 (65.0)	14 (35.0)	1.5 (1.4, 2.9)	18	7 (38.9)	11 (61.1)	5.9 (1.5, NE)	2.0723 (0.8937, 4.8052) 0.0895	0.0841	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.5072
HER2 IHC 1+	214	97 (45.3)	117 (54.7)	9.8 (7.1, 20.9)	107	33 (30.8)	74 (69.2)	11.4 (9.0, NE)	1.1913 (0.7999, 1.7742) 0.3891	0.3919	
HER2 IHC 2+/ISH Negative	159	76 (47.8)	83 (52.2)	9.0 (4.4, NE)	77	23 (29.9)	54 (70.1)	13.3 (8.6, NE)	1.5203 (0.9523, 2.4271) 0.0792	0.0782	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.9367
1	221	107 (48.4)	114 (51.6)	9.0 (5.6, 20.9)	100	32 (32.0)	68 (68.0)	13.3 (9.0, NE)	1.3388 (0.9009, 1.9896) 0.1489	0.1469
>=2	151	66 (43.7)	85 (56.3)	12.5 (5.6, NE)	83	24 (28.9)	59 (71.1)	14.4 (8.6, NE)	1.3154 (0.8214, 2.1063) 0.2539	0.2607

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.0388
Yes	235	119 (50.6)	116 (49.4)	7.6 (4.4, 10.3)	118	32 (27.1)	86 (72.9)	13.3 (9.0, NE)	1.6253 (1.0983, 2.4053) 0.0152	0.0143	
No	98	35 (35.7)	63 (64.3)	NE (16.1, NE)	48	17 (35.4)	31 (64.6)	14.4 (3.0, NE)	0.8210 (0.4579, 1.4720) 0.5079	0.5025	

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[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Common Symptoms/Diarrhea

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2880
<65	290	140 (48.3)	150 (51.7)	9.2 (5.8, 16.1)	136	39 (28.7)	97 (71.3)	13.3 (9.0, NE)	1.4364 (1.0055, 2.0520) 0.0466	0.0466	
>=65	83	33 (39.8)	50 (60.2)	14.1 (5.6, NE)	48	17 (35.4)	31 (64.6)	14.4 (4.2, NE)	1.0108 (0.5607, 1.8223) 0.9715	0.9686	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Age										0.5768
<75	359	166 (46.2)	193 (53.8)	9.6 (7.0, 20.9)	175	53 (30.3)	122 (69.7)	13.3 (9.0, NE)	1.2972 (0.9505, 1.7705) 0.1011	0.1022
>=75	14	7 (50.0)	7 (50.0)	14.1 (0.9, NE)	9	3 (33.3)	6 (66.7)	14.4 (0.8, 14.4)	1.6313 (0.4174, 6.3746) 0.4816	0.4773

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Common Symptoms/Diarrhea

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.2714
White	176	88 (50.0)	88 (50.0)	7.0 (3.0, 12.5)	91	26 (28.6)	65 (71.4)	13.3 (9.0, NE)	1.5688 (1.0098, 2.4373) 0.0451	0.0435	
Non-White	197	85 (43.1)	112 (56.9)	15.3 (8.3, NE)	92	30 (32.6)	62 (67.4)	14.4 (9.0, NE)	1.1221 (0.7386, 1.7048) 0.5892	0.5964	

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Common Symptoms/Diarrhea

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.4261
Asia	147	63 (42.9)	84 (57.1)	NE (7.6, NE)	66	23 (34.8)	43 (65.2)	14.4 (8.6, NE)	1.0510 (0.6509, 1.6972) 0.8387	0.8493	
North America	60	27 (45.0)	33 (55.0)	5.6 (3.0, 9.8)	33	8 (24.2)	25 (75.8)	13.3 (NE, NE)	1.4872 (0.6707, 3.2978) 0.3287	0.3255	
Europe + Israel	166	83 (50.0)	83 (50.0)	8.3 (3.1, 15.3)	85	25 (29.4)	60 (70.6)	11.4 (9.0, NE)	1.5670 (0.9982, 2.4601) 0.0509	0.0499	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
ECOG PS											0.3595
0	200	93 (46.5)	107 (53.5)	9.8 (7.0, NE)	105	33 (31.4)	72 (68.6)	11.4 (9.0, NE)	1.1775 (0.7902, 1.7546) 0.4220	0.4227	
1	173	80 (46.2)	93 (53.8)	9.2 (5.6, 15.3)	79	23 (29.1)	56 (70.9)	13.3 (8.6, NE)	1.5198 (0.9524, 2.4253) 0.0792	0.0790	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.2774
0	60	25 (41.7)	35 (58.3)	12.5 (5.4, NE)	34	10 (29.4)	24 (70.6)	NE (5.3, NE)	1.1898 (0.5693, 2.4869) 0.6440	0.6472	
1	108	49 (45.4)	59 (54.6)	9.6 (3.5, NE)	51	17 (33.3)	34 (66.7)	NE (4.2, NE)	1.2390 (0.7111, 2.1588) 0.4493	0.4468	
2	115	58 (50.4)	57 (49.6)	8.3 (4.4, 15.3)	54	11 (20.4)	43 (79.6)	NE (NE, NE)	2.1585 (1.1273, 4.1330) 0.0203	0.0172	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	41 (45.6)	49 (54.4)	11.3 (4.9, NE)	45	18 (40.0)	27 (60.0)	9.3 (5.1, 14.4)	0.9256 (0.5293, 1.6184) 0.7862	0.7769

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.1329
PD	174	82 (47.1)	92 (52.9)	7.6 (4.6, 14.1)	85	21 (24.7)	64 (75.3)	11.4 (11.4, NE)	1.7490 (1.0794, 2.8340) 0.0232	0.0221	
PR	48	13 (27.1)	35 (72.9)	NE (NE, NE)	22	7 (31.8)	15 (68.2)	9.0 (3.0, NE)	0.6478 (0.2562, 1.6380) 0.3590	0.3469	
SD	82	45 (54.9)	37 (45.1)	7.0 (2.8, 10.3)	55	19 (34.5)	36 (65.5)	NE (9.0, NE)	1.4537 (0.8494, 2.4879) 0.1724	0.1680	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.2413
Yes	37	18 (48.6)	19 (51.4)	9.4 (3.0, NE)	15	2 (13.3)	13 (86.7)	NE (1.5, NE)	2.7282 (0.6272, 11.8676)	0.1619
No	336	155 (46.1)	181 (53.9)	9.6 (7.0, 20.9)	169	54 (32.0)	115 (68.0)	13.3 (9.0, NE)	1.2749 (0.9338, 1.7406)	0.1281

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0185
Yes	24	12 (50.0)	12 (50.0)	9.6 (1.6, NE)	8	0	8 (100)	NE (NE, NE)	NE (NE, NE) 0.9931	0.0441	
No	349	161 (46.1)	188 (53.9)	9.7 (7.0, 20.9)	176	56 (31.8)	120 (68.2)	13.3 (9.0, NE)	1.2546 (0.9240, 1.7034) 0.1461	0.1483	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0148
Normal Function	202	100 (49.5)	102 (50.5)	8.3 (5.6, 16.1)	87	17 (19.5)	70 (80.5)	NE (13.3, NE)	2.2863 (1.3653, 3.8285) 0.0017	0.0013	
Mild Impairment	123	56 (45.5)	67 (54.5)	11.3 (5.4, NE)	69	26 (37.7)	43 (62.3)	9.0 (2.9, NE)	0.9149 (0.5690, 1.4709) 0.7135	0.7118	
Moderate Impairment	41	16 (39.0)	25 (61.0)	NE (3.0, NE)	23	11 (47.8)	12 (52.2)	11.4 (1.5, NE)	0.8667 (0.4020, 1.8690) 0.7153	0.7181	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.6547
Normal Function	170	85 (50.0)	85 (50.0)	9.0 (5.1, NE)	98	30 (30.6)	68 (69.4)	14.4 (9.0, NE)	1.4338 (0.9439, 2.1779) 0.0912	0.0900	
Mild Impairment	195	87 (44.6)	108 (55.4)	11.1 (5.6, 21.7)	84	25 (29.8)	59 (70.2)	13.3 (5.3, NE)	1.2146 (0.7754, 1.9026) 0.3959	0.3967	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline visceral disease										0.1225
Yes	332	154 (46.4)	178 (53.6)	9.6 (7.1, 16.1)	157	43 (27.4)	114 (72.6)	14.4 (11.4, NE)	1.4802 (1.0539, 2.0790) 0.0236	0.0228
No	41	19 (46.3)	22 (53.7)	7.0 (3.0, NE)	27	13 (48.1)	14 (51.9)	5.9 (1.5, NE)	0.8328 (0.4096, 1.6932) 0.6133	0.6052

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.5058
Positive	331	155 (46.8)	176 (53.2)	9.6 (7.0, 20.9)	163	47 (28.8)	116 (71.2)	14.4 (9.3, NE)	1.3861 (0.9985, 1.9240) 0.0510	0.0503	
Negative	42	18 (42.9)	24 (57.1)	8.9 (2.8, NE)	21	9 (42.9)	12 (57.1)	5.9 (3.0, NE)	1.0105 (0.4494, 2.2721) 0.9798	0.9983	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.8827
Positive	333	154 (46.2)	179 (53.8)	9.7 (7.0, 20.9)	166	49 (29.5)	117 (70.5)	14.4 (9.3, NE)	1.3419 (0.9714, 1.8537) 0.0744	0.0740	
Negative	40	19 (47.5)	21 (52.5)	7.6 (2.8, NE)	18	7 (38.9)	11 (61.1)	9.0 (3.2, NE)	1.2141 (0.5055, 2.9159) 0.6643	0.6766	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
HER2 status										0.6670
HER2 IHC 1+	214	63 (29.4)	151 (70.6)	NE (16.4, NE)	107	27 (25.2)	80 (74.8)	18.5 (11.3, 18.5)	0.7854 (0.4950, 1.2463) 0.3052	0.3032
HER2 IHC 2+/ISH Negative	159	43 (27.0)	116 (73.0)	NE (16.5, NE)	77	21 (27.3)	56 (72.7)	NE (6.1, NE)	0.7523 (0.4433, 1.2769) 0.2917	0.2869

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.7850
1	221	60 (27.1)	161 (72.9)	NE (NE, NE)	100	26 (26.0)	74 (74.0)	NE (11.3, NE)	0.8257 (0.5184, 1.3152) 0.4201	0.4196
>=2	151	45 (29.8)	106 (70.2)	NE (13.6, NE)	83	22 (26.5)	61 (73.5)	18.5 (6.1, 18.5)	0.6825 (0.4034, 1.1548) 0.1546	0.1509

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.5651
Yes	235	61 (26.0)	174 (74.0)	NE (16.5, NE)	118	29 (24.6)	89 (75.4)	18.5 (18.5, NE)	0.7626 (0.4865, 1.1953) 0.2372	0.2357	
No	98	35 (35.7)	63 (64.3)	NE (12.0, NE)	48	13 (27.1)	35 (72.9)	NE (9.3, NE)	0.9665 (0.5054, 1.8484) 0.9180	0.9105	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]	
Age										0.4081	
<65	290	85 (29.3)	205 (70.7)	NE (16.5, NE)	136	38 (27.9)	98 (72.1)	NE (6.9, NE)	0.7276 (0.4930, 1.0737)	0.1063	
>=65	83	21 (25.3)	62 (74.7)	NE (11.7, NE)	48	10 (20.8)	38 (79.2)	18.5 (11.3, 18.5)	0.8749 (0.4040, 1.8946)	0.7365	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]	
Age										0.5801	
<75	359	101 (28.1)	258 (71.9)	NE (NE, NE)	175	45 (25.7)	130 (74.3)	18.5 (18.5, NE)	0.7596 (0.5309, 1.0870)	0.1305	
>=75	14	5 (35.7)	9 (64.3)	NE (1.6, NE)	9	3 (33.3)	6 (66.7)	11.3 (1.4, NE)	1.1756 (0.2798, 4.9388)	0.8250	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Race										0.8717
White	176	48 (27.3)	128 (72.7)	NE (NE, NE)	91	23 (25.3)	68 (74.7)	18.5 (6.0, 18.5)	0.7936 (0.4778, 1.3181) 0.3718	0.3698
Non-White	197	58 (29.4)	139 (70.6)	NE (16.5, NE)	92	25 (27.2)	67 (72.8)	NE (9.3, NE)	0.7531 (0.4670, 1.2142) 0.2445	0.2431

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.7647
Asia	147	49 (33.3)	98 (66.7)	NE (14.3, NE)	66	20 (30.3)	46 (69.7)	NE (9.3, NE)	0.7521 (0.4431, 1.2768) 0.2915	0.2915	
North America	60	11 (18.3)	49 (81.7)	NE (NE, NE)	33	7 (21.2)	26 (78.8)	NE (2.7, NE)	0.6969 (0.2677, 1.8143) 0.4595	0.4555	
Europe + Israel	166	46 (27.7)	120 (72.3)	NE (NE, NE)	85	21 (24.7)	64 (75.3)	18.5 (NE, NE)	0.8451 (0.4986, 1.4322) 0.5317	0.5277	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
ECOG PS										0.7928
0	200	57 (28.5)	143 (71.5)	NE (16.5, NE)	105	25 (23.8)	80 (76.2)	18.5 (18.5, NE)	0.8202 (0.5089, 1.3218)	0.4157
1	173	49 (28.3)	124 (71.7)	NE (13.6, NE)	79	23 (29.1)	56 (70.9)	11.3 (6.9, NE)	0.7038 (0.4229, 1.1715)	0.1731

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)									0.0673
0	60	15 (25.0)	45 (75.0) (10.4, NE)	34	9 (26.5)	25 (73.5) (5.9, NE)	0.4971 (0.2088, 1.1837) 0.1144	0.1077	
1	108	30 (27.8)	78 (72.2) (12.0, NE)	51	15 (29.4)	36 (70.6) (6.1, 18.5)	0.7707 (0.4122, 1.4410) 0.4146	0.4116	
2	115	29 (25.2)	86 (74.8) (NE, NE)	54	17 (31.5)	37 (68.5) (5.1, NE)	0.5641 (0.3057, 1.0410) 0.0671	0.0633	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.3.5.2 - EORTC QLQ-C30 - First deterioration - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	32 (35.6)	58 (64.4)	NE (11.3, NE)	45	7 (15.6)	38 (84.4)	NE (NE, NE)	1.7357 (0.7590, 3.9694) 0.1914	0.1865

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 15SEP2022 – 12:00; Program name: T3\_EQ5D\_FD\_2\_FAS.sas; Output name: T3\_EORTCC30\_FD\_2\_FAS.rtf



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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.8535
PD	174	44 (25.3)	130 (74.7)	NE (16.5, NE)	85	22 (25.9)	63 (74.1)	18.5 (6.9, 18.5)	0.7307 (0.4334, 1.2319) 0.2391	0.2341	
PR	48	17 (35.4)	31 (64.6)	NE (10.4, NE)	22	5 (22.7)	17 (77.3)	NE (1.7, NE)	0.8808 (0.3201, 2.4232) 0.8058	0.8123	
SD	82	24 (29.3)	58 (70.7)	NE (13.1, NE)	55	17 (30.9)	38 (69.1)	11.3 (6.1, NE)	0.6482 (0.3438, 1.2220) 0.1801	0.1778	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.3.5.2 - EORTC QLQ-C30 - First deterioration - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]	
Reported history of CNS metastases										0.1474	
Yes	37	10 (27.0)	27 (73.0)	NE (8.8, NE)	15	1 (6.7)	14 (93.3)	NE (NE, NE)	2.7337 (0.3451, 21.6577)	0.3210	
No	336	96 (28.6)	240 (71.4)	NE (16.5, NE)	169	47 (27.8)	122 (72.2)	18.5 (11.3, NE)	0.7226 (0.5059, 1.0322)	0.0723	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Baseline CNS metastases											
Yes	24	6 (25.0)	18 (75.0)	16.5 (7.1, NE)	8	0	8 (100)	NE (NE, NE)	0.9955	0.2048	0.0540
No	349	100 (28.7)	249 (71.3)	NE (NE, NE)	176	48 (27.3)	128 (72.7)	18.5 (11.3, NE)	0.7456 (0.5248, 1.0593)	0.1014	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 15SEP2022 – 12:00; Program name: T3\_EQ5D\_FD\_2\_FAS.sas; Output name: T3\_EORTCC30\_FD\_2\_FAS.rtf

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.2506
Normal Function	202	64 (31.7)	138 (68.3)	NE (16.5, NE)	87	23 (26.4)	64 (73.6)	NE (9.3, NE)	0.8916 (0.5503, 1.4445) 0.6412	0.6369	
Mild Impairment	123	29 (23.6)	94 (76.4)	NE (14.3, NE)	69	19 (27.5)	50 (72.5)	NE (6.0, NE)	0.4601 (0.2498, 0.8474) 0.0127	0.0112	
Moderate Impairment	41	12 (29.3)	29 (70.7)	NE (11.2, NE)	23	6 (26.1)	17 (73.9)	18.5 (7.0, 18.5)	1.0841 (0.4036, 2.9123) 0.8727	0.8741	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]	
Hepatic function at baseline										0.4083	
Normal Function	170	52 (30.6)	118 (69.4)	NE (16.5, NE)	98	30 (30.6)	68 (69.4)	NE (6.9, NE)	0.6850 (0.4333, 1.0831)	0.1033	
Mild Impairment	195	54 (27.7)	141 (72.3)	NE (16.4, NE)	84	18 (21.4)	66 (78.6)	18.5 (11.3, 18.5)	0.9174 (0.5327, 1.5797)	0.7507	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline visceral disease										0.0686
Yes	332	94 (28.3)	238 (71.7)	NE (NE, NE)	157	37 (23.6)	120 (76.4)	18.5 (11.3, NE)	0.8930 (0.6072, 1.3133) 0.5652	0.5623
No	41	12 (29.3)	29 (70.7)	NE (13.1, NE)	27	11 (40.7)	16 (59.3)	5.9 (1.7, NE)	0.3395 (0.1394, 0.8268) 0.0174	0.0130

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 15SEP2022 – 12:00; Program name: T3\_EQ5D\_FD\_2\_FAS.sas; Output name: T3\_EORTCC30\_FD\_2\_FAS.rtf

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)										0.4571	
Positive	331	95 (28.7)	236 (71.3)	NE (NE, NE)	163	41 (25.2)	122 (74.8)	18.5 (11.3, NE)	0.8198 (0.5648, 1.1898)	0.2930	
Negative	42	11 (26.2)	31 (73.8)	NE (8.3, NE)	21	7 (33.3)	14 (66.7)	7.0 (4.4, NE)	0.4678 (0.1725, 1.2684)	0.1253	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.5019
Positive	333	95 (28.5)	238 (71.5)	NE (NE, NE)	166	42 (25.3)	124 (74.7)	18.5 (11.3, NE)	0.8129 (0.5617, 1.1766)	0.2695	
Negative	40	11 (27.5)	29 (72.5)	NE (8.3, NE)	18	6 (33.3)	12 (66.7)	7.0 (1.7, NE)	0.4656 (0.1652, 1.3122)	0.1375	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

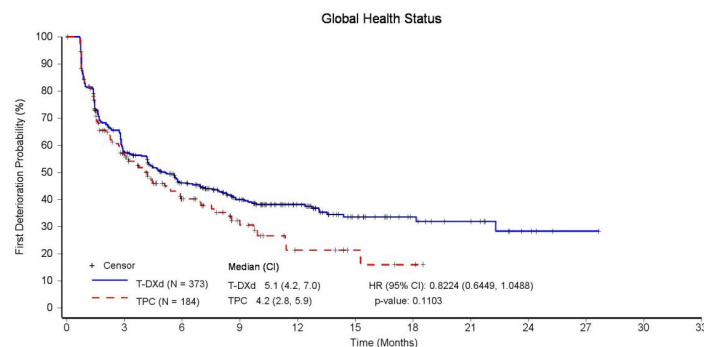
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 Run date: 15SEP2022 – 12:00; Program name: T3\_EQ5D\_FD\_2\_FAS.sas; Output name: T3\_EORTCC30\_FD\_2\_FAS.rtf



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Patients still at risk:

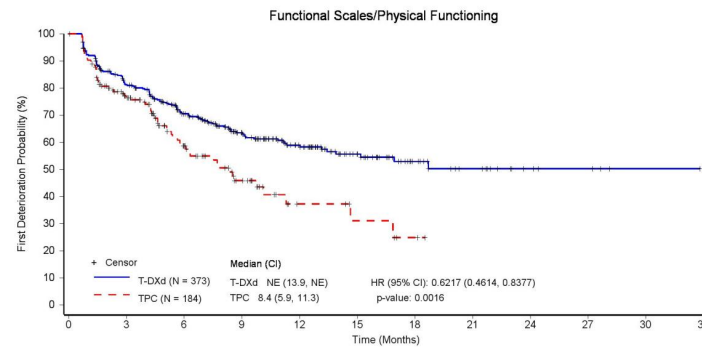
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	193	135	93	60	34	20	13	4	1	0	0
TPC (N = 184)	184	77	38	19	7	4	2	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

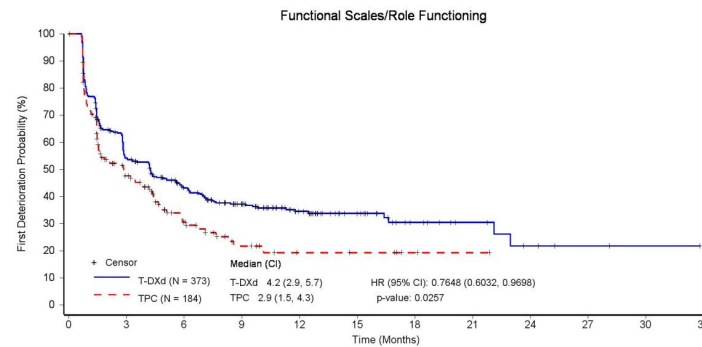
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	267	197	143	89	51	26	15	6	4	1	0
TPC (N = 184)	184	102	52	26	8	5	2	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:12; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F3\_EORTCC30\_FD\_3\_FAS.rf

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Patients still at risk:

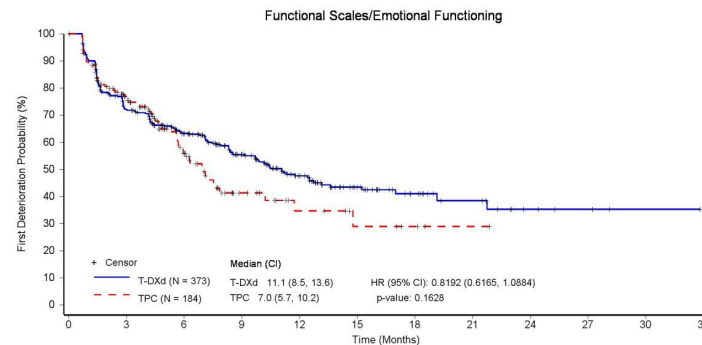
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	178	120	84	48	27	14	8	4	2	1	0
TPC (N = 184)	184	61	26	12	6	5	2	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:12; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F3\_EORTCC30\_FD\_3\_FAS.rf

Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.3.5.3 - EORTC QLQ-C30 - First deterioration - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

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Patients still at risk:

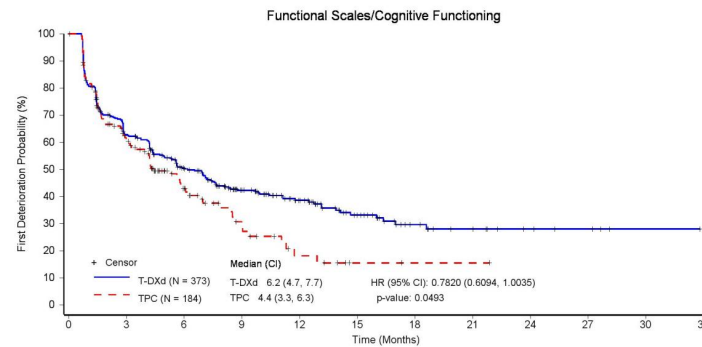
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	240	183	128	79	44	26	14	5	3	1	0
TPC (N = 184)	184	100	47	18	9	5	3	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:12; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F3\_EORTCC30\_FD\_3\_FAS.rf

Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	206	144	95	62	35	19	11	6	4	1	0
TPC (N = 184)	184	85	37	17	7	2	1	1	0	0	0	0

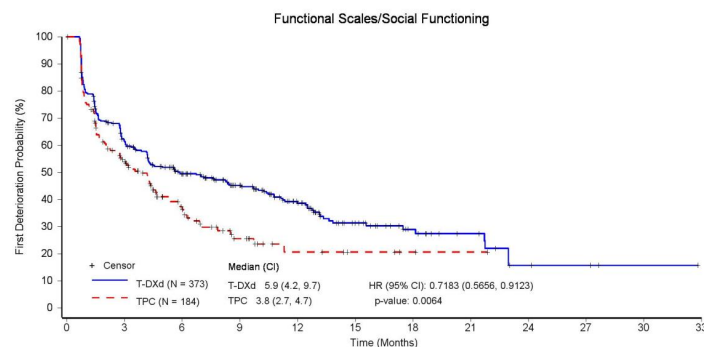
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:12; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F3\_EORTCC30\_FD\_3\_FAS.rf

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DE.F.3.5.3 - EORTC QLQ-C30 - First deterioration - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	203	143	105	64	33	19	11	4	3	1	0
TPC (N = 184)	184	79	38	16	7	4	2	1	0	0	0	0

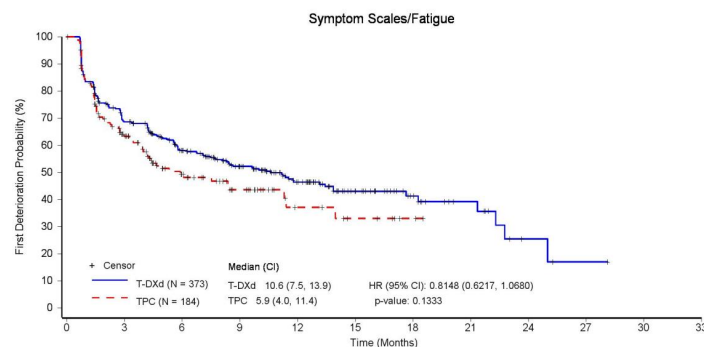
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:12; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F3\_EORTCC30\_FD\_3\_FAS.rf

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DE.F.3.5.3 - EORTC QLQ-C30 - First deterioration - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	226	164	122	75	40	21	11	3	1	0	0
TPC (N = 184)	184	84	43	25	10	6	2	0	0	0	0	0

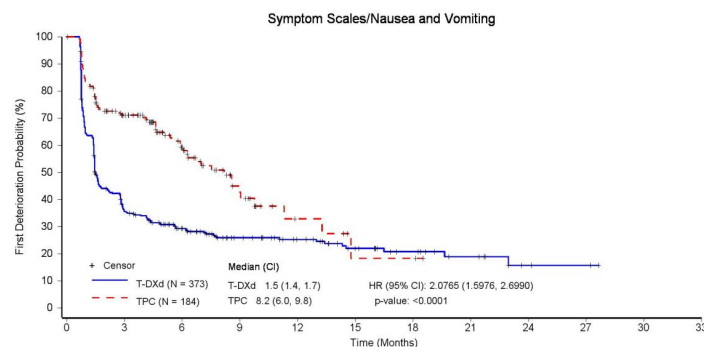
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:12; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F3\_EORTCC30\_FD\_3\_FAS.rf

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DE.F.3.5.3 - EORTC QLQ-C30 - First deterioration - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	116	77	48	36	23	15	9	3	2	0	0
TPC (N = 184)	184	94	50	20	6	2	2	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

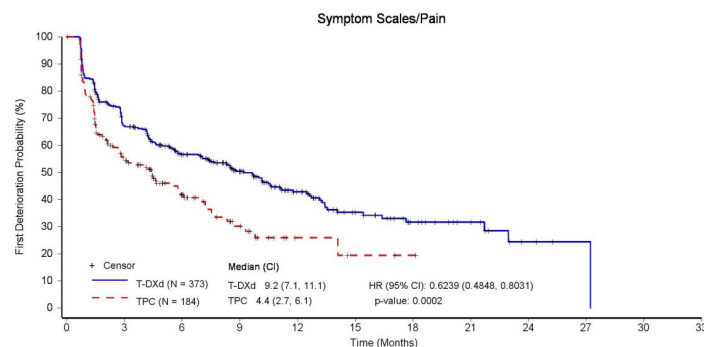
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DE.F.3.5.3 - EORTC QLQ-C30 - First deterioration - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	220	156	108	62	33	20	12	3	1	0	0
TPC (N = 184)	184	78	38	17	4	2	1	0	0	0	0	0

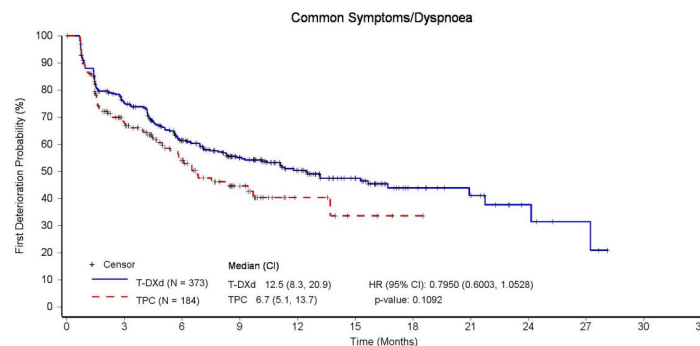
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

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 Run date: 21OCT2022 – 18:12; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F3\_EORTCC30\_FD\_3\_FAS.rf

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DE.F.3.5.3 - EORTC QLQ-C30 - First deterioration - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

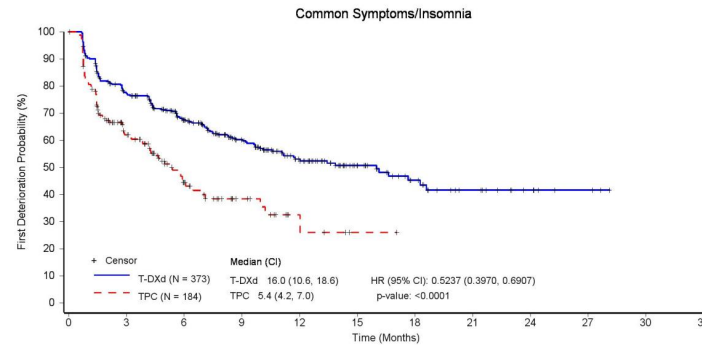
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	248	172	123	81	50	23	15	6	3	0	0
TPC (N = 184)	184	89	47	24	7	3	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:12; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F3\_EORTCC30\_FD\_3\_FAS.rf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.3.5.3 - EORTC QLQ-C30 - First deterioration - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

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Patients still at risk:

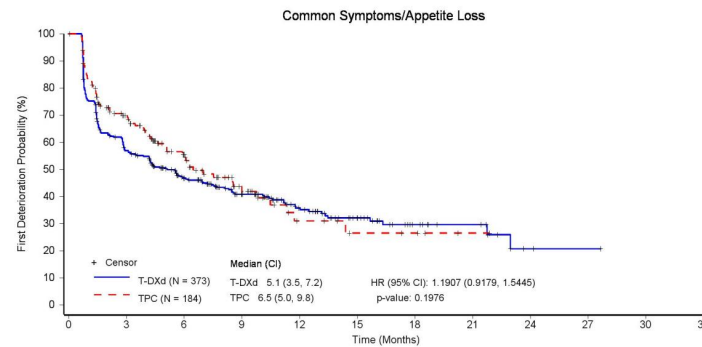
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	256	187	130	82	47	27	14	7	3	0	0
TPC (N = 184)	184	80	35	15	5	1	0	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:12; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F3\_EORTCC30\_FD\_3\_FAS.rf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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Patients still at risk:

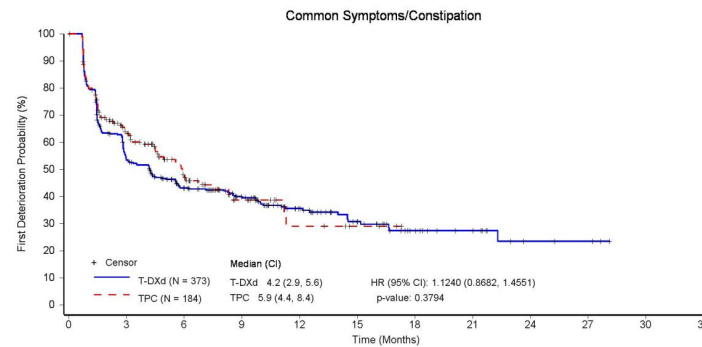
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	192	132	92	55	32	16	10	2	1	0	0
TPC (N = 184)	184	94	50	23	9	5	4	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:12; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F3\_EORTCC30\_FD\_3\_FAS.rf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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Patients still at risk:

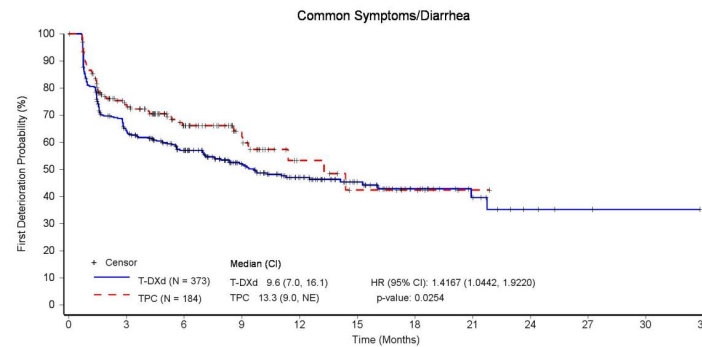
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	177	120	92	56	33	18	12	4	3	0	0
TPC (N = 184)	184	83	42	16	6	3	0	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:12; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F3\_EORTCC30\_FD\_3\_FAS.rf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.3.5.3 - EORTC QLQ-C30 - First deterioration - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

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Patients still at risk:

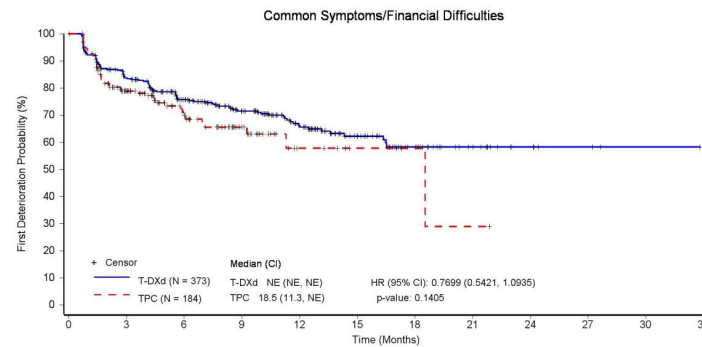
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	209	159	110	71	40	22	12	4	2	1	0
TPC (N = 184)	184	95	53	29	11	6	4	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:12; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F3\_EORTCC30\_FD\_3\_FAS.rf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.3.5.3 - EORTC QLQ-C30 - First deterioration - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

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Patients still at risk:

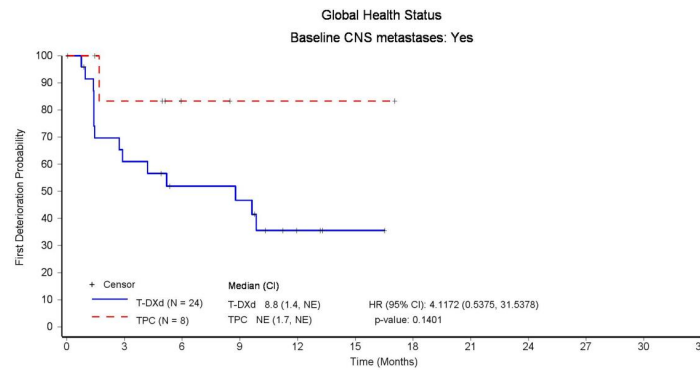
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	269	204	152	99	58	33	15	6	3	1	0
TPC (N = 184)	184	104	57	28	8	4	2	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:12; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F3\_EORTCC30\_FD\_3\_FAS.rf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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 DE.F.3.5.4 - EORTC QLQ-C30 - First deterioration - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 24)	24	14	10	9	3	1	0	0	0	0	0	0
TPC (N = 8)	8	5	2	1	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

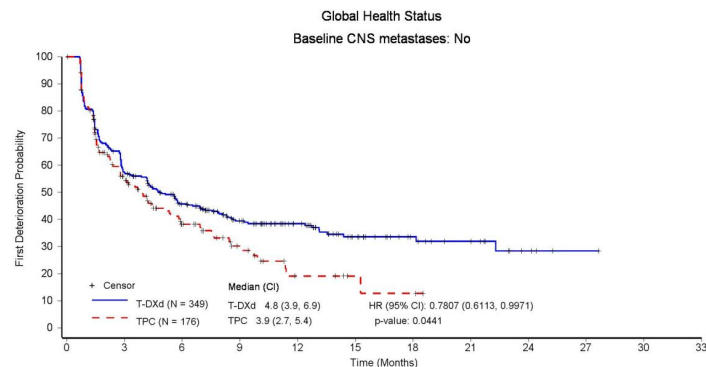
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 Run date: 21OCT2022 – 18:13; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_FD\_4\_FAS.rf



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DE.F.3.5.4 - EORTC QLQ-C30 - First deterioration - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 349)	349	179	125	84	57	33	20	13	4	1	0	0
TPC (N = 176)	176	72	36	18	6	3	2	0	0	0	0	0

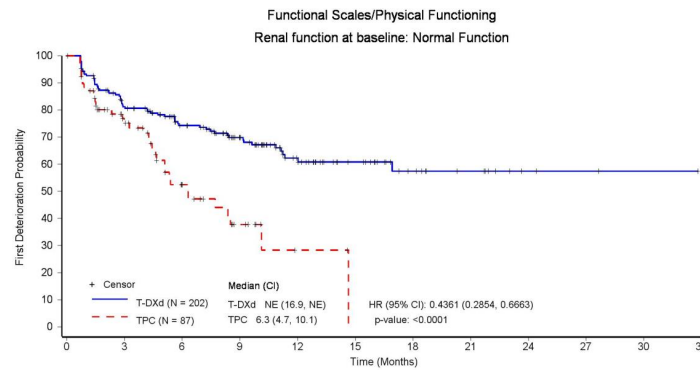
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.3.5.4 - EORTC QLQ-C30 - First deterioration - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 202)	202	145	109	81	43	27	15	9	3	2	1	0
TPC (N = 87)	87	44	21	9	2	0	0	0	0	0	0	0

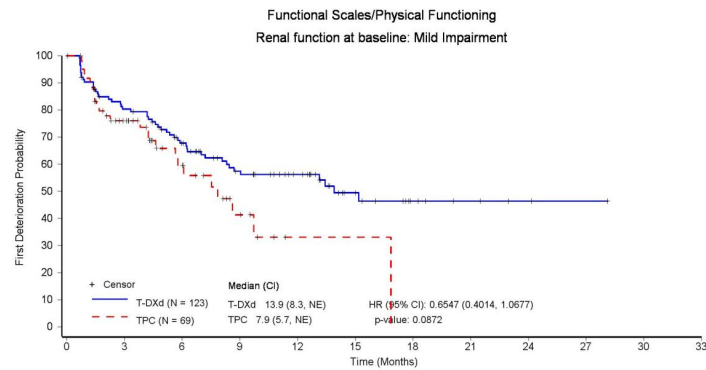
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:13; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_FD\_4\_FAS.rf

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DE.F.3.5.4 - EORTC QLQ-C30 - First deterioration - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 123)	123	87	66	46	35	17	8	5	2	1	0	0
TPC (N = 69)	69	37	19	7	1	1	0	0	0	0	0	0

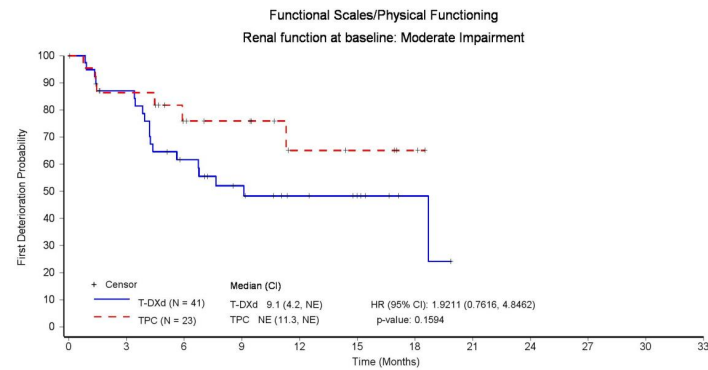
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:13; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_FD\_4\_FAS.rf

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DE.F.3.5.4 - EORTC QLQ-C30 - First deterioration - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 41)	41	31	20	14	9	6	2	0	0	0	0	0
TPC (N = 23)	23	19	12	10	5	4	2	0	0	0	0	0

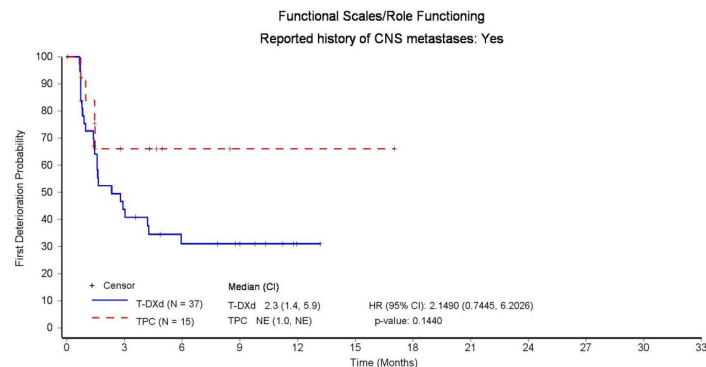
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.3.5.4 - EORTC QLQ-C30 - First deterioration - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

T-DXd (N = 37)	37	15	9	7	1	0	0	0	0	0	0
TPC (N = 15)	15	5	2	1	1	1	0	0	0	0	0

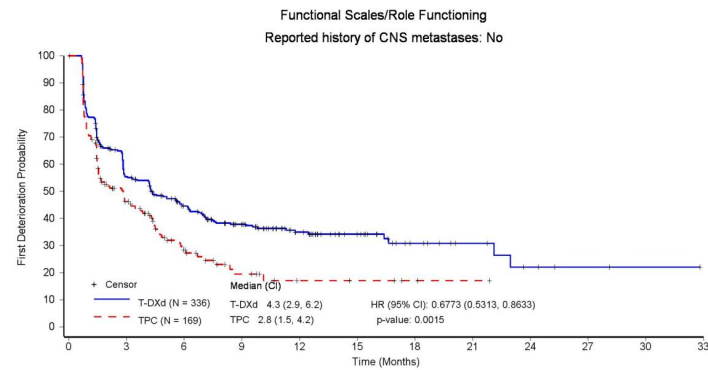
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:13; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_FD\_4\_FAS.rf

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DE.F.3.5.4 - EORTC QLQ-C30 - First deterioration - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 336)	336	163	111	77	47	27	14	8	4	2	1	0
TPC (N = 169)	169	56	24	11	5	4	2	1	0	0	0	0

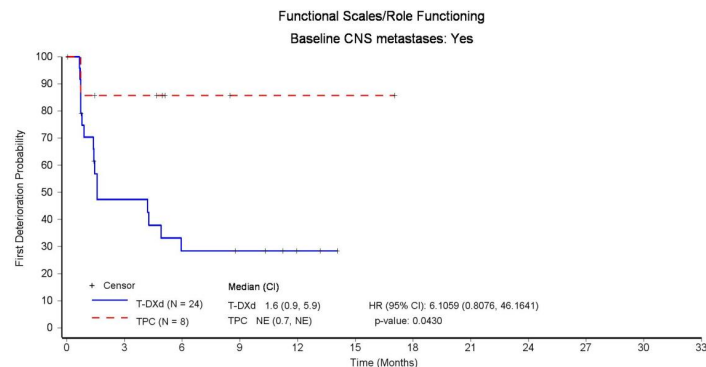
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:13; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_FD\_4\_FAS.rf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 24)	24	10	6	5	2	0	0	0	0	0	0	0
TPC (N = 8)	8	5	2	1	1	1	0	0	0	0	0	0

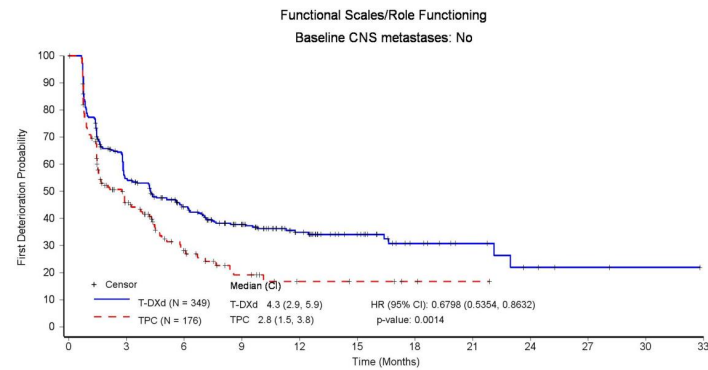
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:13; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_FD\_4\_FAS.rf

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DE.F.3.5.4 - EORTC QLQ-C30 - First deterioration - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 349)	349	168	114	79	46	27	14	8	4	2	1	0
TPC (N = 176)	176	56	24	11	5	4	2	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

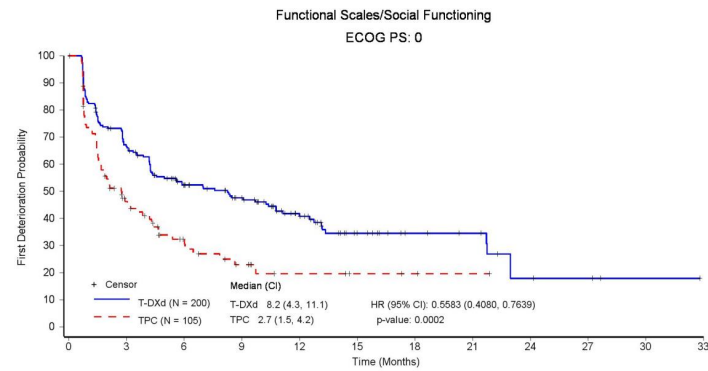
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 Run date: 21OCT2022 – 18:13; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_FD\_4\_FAS.rf



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DE.F.3.5.4 - EORTC QLQ-C30 - First deterioration - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 200)	200	121	84	66	40	20	13	10	4	3	1	0
TPC (N = 105)	105	36	18	10	5	3	2	1	0	0	0	0

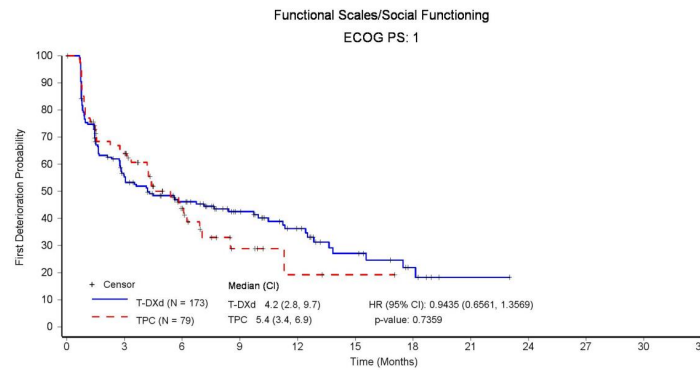
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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 Run date: 21OCT2022 – 18:13; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_FD\_4\_FAS.rf

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Patients still at risk:

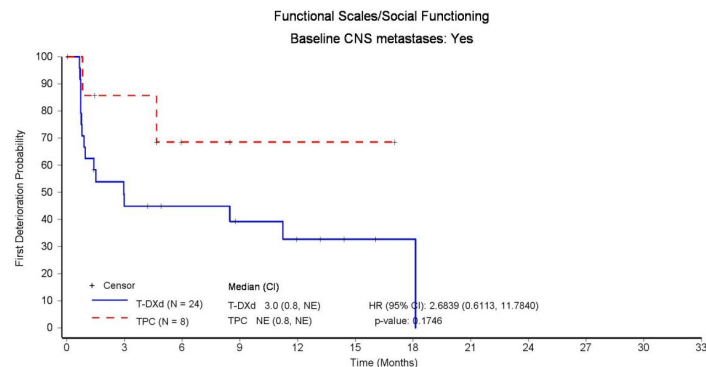
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 173)	173	82	59	39	24	13	6	1	0	0	0	0
TPC (N = 79)	79	43	20	6	2	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:13; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_FD\_4\_FAS.rf

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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 24)	24	10	8	6	4	2	1	0	0	0	0	0
TPC (N = 8)	8	5	2	1	1	1	0	0	0	0	0	0

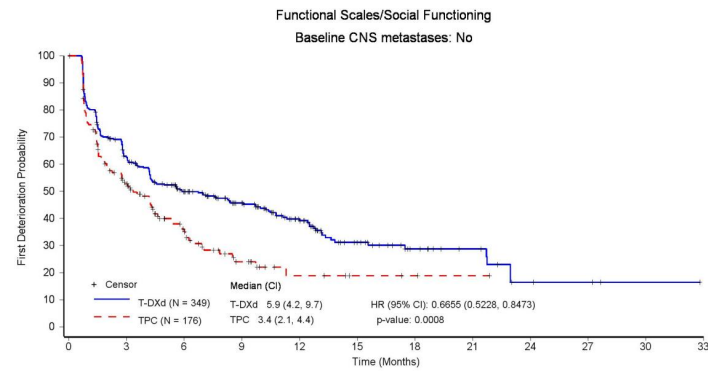
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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 Run date: 21OCT2022 – 18:13; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_FD\_4\_FAS.rf

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Patients still at risk:

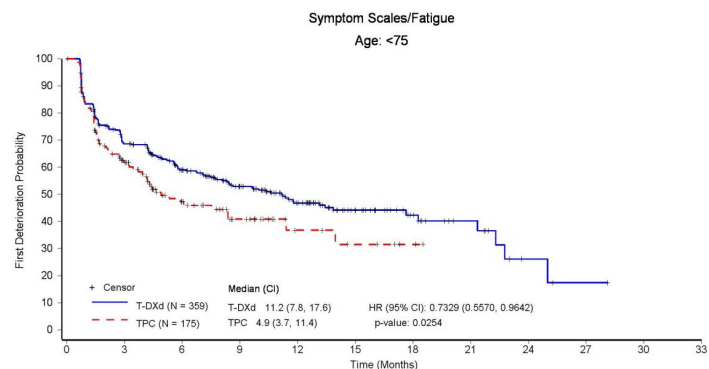
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 349)	349	193	135	99	60	31	18	11	4	3	1	0
TPC (N = 176)	176	74	36	15	6	3	2	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:13; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_FD\_4\_FAS.rf

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Patients still at risk:

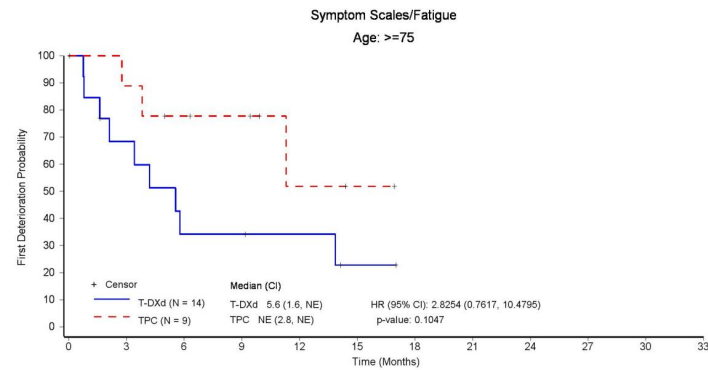
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 359)	359	218	160	118	72	39	21	11	3	1	0	0
TPC (N = 175)	175	76	37	20	8	5	2	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

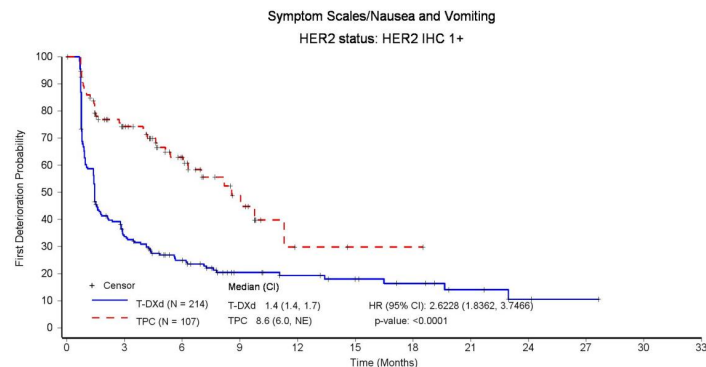
T-DXd (N = 14)	14	8	4	4	3	1	0	0	0	0	0
TPC (N = 9)	9	8	6	5	2	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:13; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_FD\_4\_FAS.rf

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Patients still at risk:

T-DXd (N = 214)	214	61	38	20	16	12	9	5	2	1	0	0
TPC (N = 107)	107	54	31	12	2	1	1	0	0	0	0	0

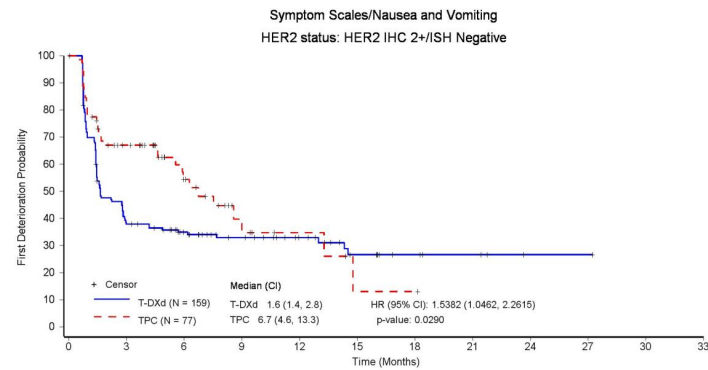
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:13; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_FD\_4\_FAS.rf

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DE.F.3.5.4 - EORTC QLQ-C30 - First deterioration - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 159)	159	55	39	28	20	11	6	4	1	1	0	0
TPC (N = 77)	77	40	19	8	4	1	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

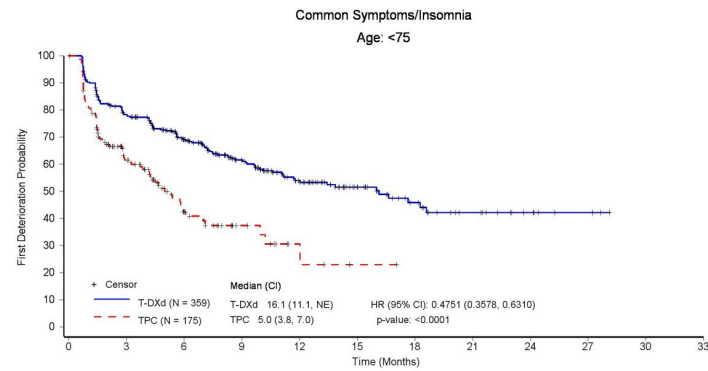
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Patients still at risk:

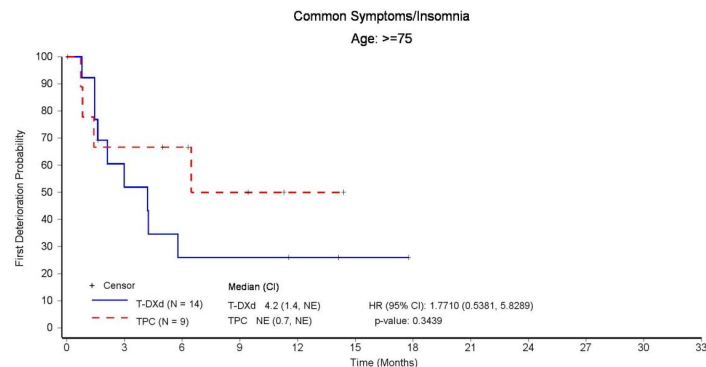
T-DXd (N = 359)	359	249	184	127	80	46	27	14	7	3	0	0
TPC (N = 175)	175	74	30	12	4	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:13; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_FD\_4\_FAS.rf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 14)	14	6	3	3	2	1	0	0	0	0	0	0
TPC (N = 9)	9	6	5	3	1	0	0	0	0	0	0	0

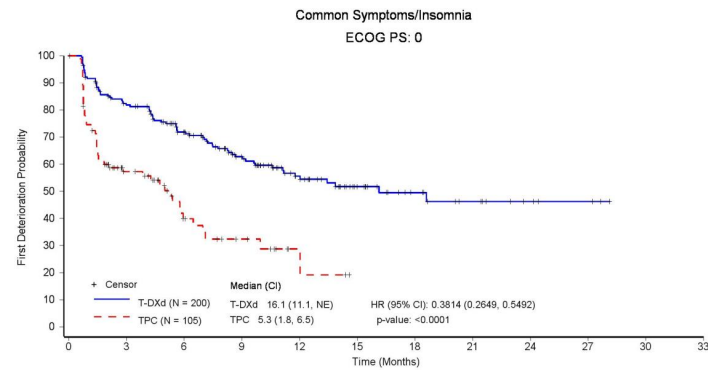
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.3.5.4 - EORTC QLQ-C30 - First deterioration - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 200)	200	148	113	80	49	28	17	10	5	3	0	0
TPC (N = 105)	105	38	17	10	3	0	0	0	0	0	0	0

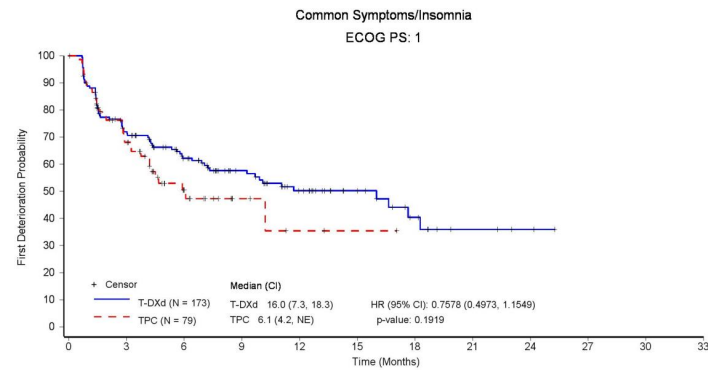
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

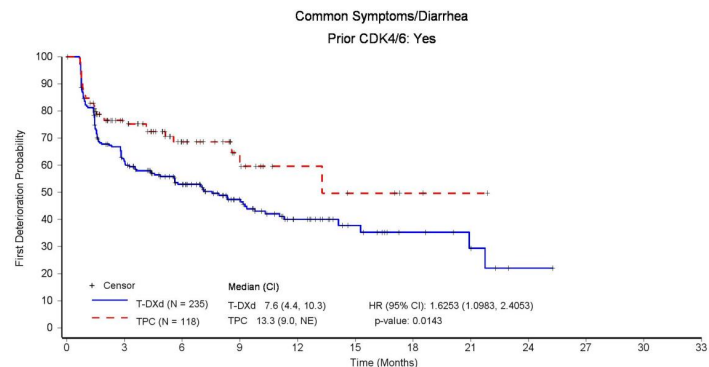
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 173)	173	107	74	50	33	19	10	4	2	0	0	0
TPC (N = 79)	79	42	18	5	2	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 235)	235	126	90	56	30	15	8	5	1	0	0	0
TPC (N = 118)	118	59	30	13	6	4	2	1	0	0	0	0

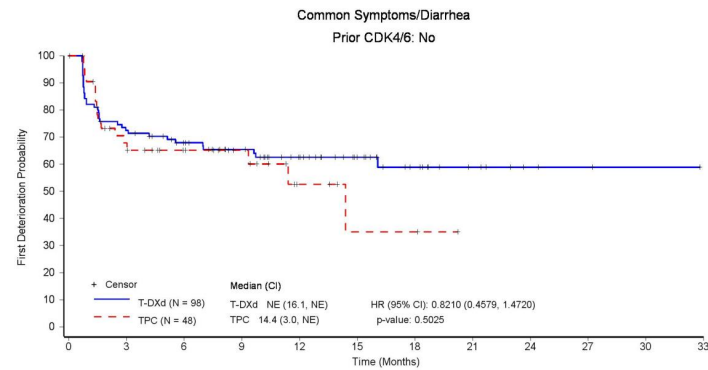
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:13; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_FD\_4\_FAS.rf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 98)	98	67	56	47	35	22	13	7	3	2	1	0
TPC (N = 48)	48	25	18	13	5	2	2	0	0	0	0	0

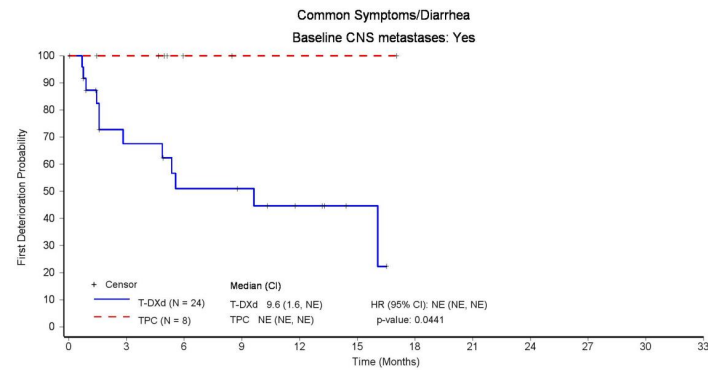
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

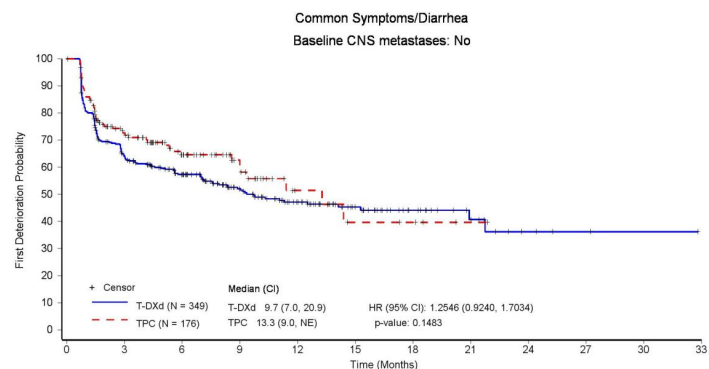
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 24)	24	13	9	8	5	2	0	0	0	0	0	0
TPC (N = 8)	8	6	2	1	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:13; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_FD\_4\_FAS.rf

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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 349)	349	196	150	102	66	38	22	12	4	2	1	0
TPC (N = 176)	176	89	51	28	10	5	4	1	0	0	0	0

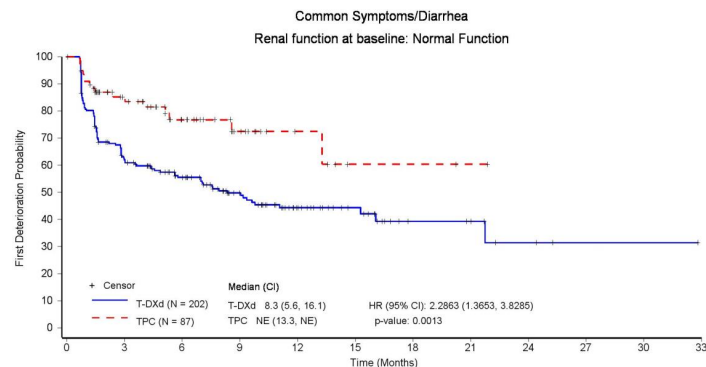
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:13; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_FD\_4\_FAS.rf



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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 202)	202	113	86	57	32	20	8	7	3	1	1	0
TPC (N = 87)	87	48	26	14	6	2	2	1	0	0	0	0

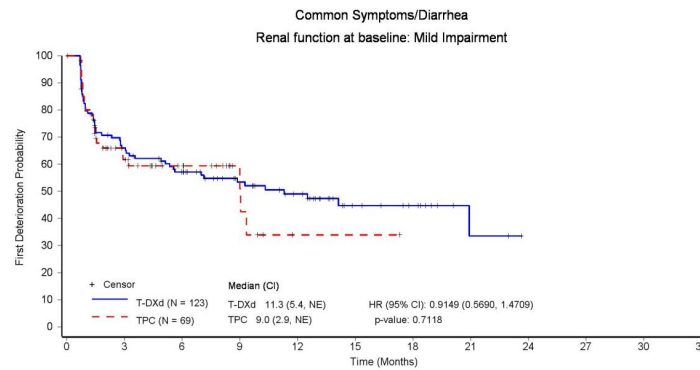
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:13; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_FD\_4\_FAS.rf

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Patients still at risk:

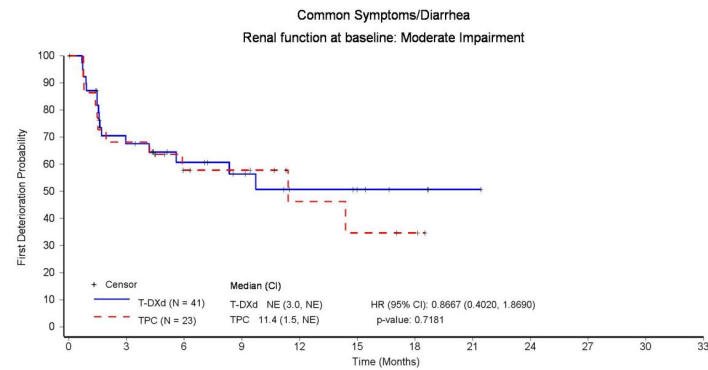
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 123)	123	69	55	39	30	14	10	3	0	0	0	0
TPC (N = 69)	69	29	17	7	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

T-DXd (N = 41)	41	23	16	12	7	5	3	1	0	0	0	0
TPC (N = 23)	23	15	9	8	4	3	2	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:13; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_FD\_4\_FAS.rf

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#### Global Health Status

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	160 (42.9)	77 (41.8)	
Number of subjects censored, n (%)	213 (57.1)	107 (58.2)	
Median time to first event (months) [a]	14.4	8.4	
95% Confidence Interval	[9.8, 18.4]	[5.9, 10.8]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.6851
95% Confidence Interval			[0.5174, 0.9073]
p-value			0.0083
Stratified log-rank p-value [c]			0.0078

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 15SEP2022 – 12:07; Program name: T3\_EQ5D\_FD\_1\_FAS.sas; Output name: T3\_EORTCC30\_DD\_1\_FAS.rtf

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Functional Scales/Physical Functioning

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	90 (24.1)	57 (31.0)	
Number of subjects censored, n (%)	283 (75.9)	127 (69.0)	
Median time to first event (months) [a]	NE	10.2	
95% Confidence Interval	[NE, NE]	[7.9, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.4818
95% Confidence Interval			[0.3415, 0.6798]
p-value			<0.0001
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Functional Scales/Role Functioning

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	159 (42.6)	86 (46.7)	
Number of subjects censored, n (%)	214 (57.4)	98 (53.3)	
Median time to first event (months) [a]	16.0	5.8	
95% Confidence Interval	[9.8, 21.5]	[4.3, 7.7]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.5733
95% Confidence Interval			[0.4367, 0.7527]
p-value			0.0001
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Functional Scales/Emotional Functioning

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	120 (32.2)	48 (26.1)	
Number of subjects censored, n (%)	253 (67.8)	136 (73.9)	
Median time to first event (months) [a]	21.7	11.7	
95% Confidence Interval	[16.7, NE]	[8.4, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.7681
95% Confidence Interval			[0.5425, 1.0876]
p-value			0.1371
Stratified log-rank p-value [c]			0.1369

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Functional Scales/Cognitive Functioning

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	157 (42.1)	82 (44.6)	
Number of subjects censored, n (%)	216 (57.9)	102 (55.4)	
Median time to first event (months) [a]	13.6	6.9	
95% Confidence Interval	[10.8, 17.5]	[5.4, 9.0]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.6015
95% Confidence Interval			[0.4557, 0.7940]
p-value			0.0003
Stratified log-rank p-value [c]			0.0003

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Functional Scales/Social Functioning

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	156 (41.8)	88 (47.8)	
Number of subjects censored, n (%)	217 (58.2)	96 (52.2)	
Median time to first event (months) [a]	13.6	6.0	
95% Confidence Interval	[11.3, 18.2]	[4.6, 7.9]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.5917
95% Confidence Interval			[0.4509, 0.7765]
p-value			0.0002
Stratified log-rank p-value [c]			0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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#### Symptom Scales/Fatigue

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	119 (31.9)	59 (32.1)	
Number of subjects censored, n (%)	254 (68.1)	125 (67.9)	
Median time to first event (months) [a]	20.7	11.4	
95% Confidence Interval	[17.8, NE]	[7.7, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.6461
95% Confidence Interval			[0.4671, 0.8936]
p-value			0.0083
Stratified log-rank p-value [c]			0.0075

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 15SEP2022 – 12:07; Program name: T3\_EQ5D\_FD\_1\_FAS.sas; Output name: T3\_EORTCC30\_DD\_1\_FAS.rtf

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Symptom Scales/Nausea and Vomiting

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	187 (50.1)	58 (31.5)	
Number of subjects censored, n (%)	186 (49.9)	126 (68.5)	
Median time to first event (months) [a]	7.5	11.3	
95% Confidence Interval	[4.4, 10.4]	[8.6, 21.9]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			1.5735
95% Confidence Interval			[1.1664, 2.1227]
p-value			0.0030
Stratified log-rank p-value [c]			0.0030

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Symptom Scales/Pain

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	128 (34.3)	80 (43.5)	
Number of subjects censored, n (%)	245 (65.7)	104 (56.5)	
Median time to first event (months) [a]	18.2	7.2	
95% Confidence Interval	[15.7, 23.0]	[4.7, 8.7]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.4265
95% Confidence Interval			[0.3168, 0.5743]
p-value			<0.0001
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Common Symptoms/Dyspnoea

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	122 (32.7)	47 (25.5)	
Number of subjects censored, n (%)	251 (67.3)	137 (74.5)	
Median time to first event (months) [a]	21.7	NE	
95% Confidence Interval	[15.9, NE]	[9.4, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.8744
95% Confidence Interval			[0.6197, 1.2339]
p-value			0.4449
Stratified log-rank p-value [c]			0.4410

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Common Symptoms/Insomnia

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	108 (29.0)	60 (32.6)	
Number of subjects censored, n (%)	265 (71.0)	124 (67.4)	
Median time to first event (months) [a]	NE	10.0	
95% Confidence Interval	[18.3, NE]	[6.9, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.5634
95% Confidence Interval			[0.4066, 0.7806]
p-value			0.0006
Stratified log-rank p-value [c]			0.0005

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Common Symptoms/Appetite Loss

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	160 (42.9)	62 (33.7)	
Number of subjects censored, n (%)	213 (57.1)	122 (66.3)	
Median time to first event (months) [a]	13.6	11.3	
95% Confidence Interval	[10.4, 22.3]	[8.5, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.9955
95% Confidence Interval			[0.7385, 1.3417]
p-value			0.9762
Stratified log-rank p-value [c]			0.9563

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Common Symptoms/Constipation

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	155 (41.6)	55 (29.9)	
Number of subjects censored, n (%)	218 (58.4)	129 (70.1)	
Median time to first event (months) [a]	13.6	11.3	
95% Confidence Interval	[10.1, NE]	[8.3, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			1.1670
95% Confidence Interval			[0.8537, 1.5952]
p-value			0.3330
Stratified log-rank p-value [c]			0.3382

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Common Symptoms/Diarrhea

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	101 (27.1)	36 (19.6)	
Number of subjects censored, n (%)	272 (72.9)	148 (80.4)	
Median time to first event (months) [a] 95% Confidence Interval	NE [21.7, NE]	NE [11.4, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.0605 [0.7202, 1.5617] 0.7659
Stratified log-rank p-value [c]			0.7750

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Common Symptoms/Financial Difficulties

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	79 (21.2)	42 (22.8)	
Number of subjects censored, n (%)	294 (78.8)	142 (77.2)	
Median time to first event (months) [a]	28.1	17.5	
95% Confidence Interval	[28.1, NE]	[11.3, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.5917
95% Confidence Interval			[0.4011, 0.8727]
p-value			0.0081
Stratified log-rank p-value [c]			0.0074

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Global Health Status

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.5025
HER2 IHC 1+	214	91 (42.5)	123 (57.5)	14.4 (8.8, 20.8)	107	48 (44.9)	59 (55.1)	6.9 (4.4, 9.9)	0.6362 (0.4453, 0.9090) 0.0130	0.0119	
HER2 IHC 2+/ISH Negative	159	69 (43.4)	90 (56.6)	15.7 (9.8, 18.6)	77	29 (37.7)	48 (62.3)	9.0 (5.9, NE)	0.7659 (0.4905, 1.1959) 0.2408	0.2379	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Global Health Status

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.2852
1	221	103 (46.6)	118 (53.4)	11.1 (8.8, 18.0)	100	40 (40.0)	60 (60.0)	9.0 (6.5, 11.4)	0.7685 (0.5287, 1.1170) 0.1675	0.1622
>=2	151	57 (37.7)	94 (62.3)	18.4 (11.3, NE)	83	37 (44.6)	46 (55.4)	6.9 (4.4, 9.9)	0.5935 (0.3891, 0.9052) 0.0154	0.0141

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Global Health Status

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.8112
Yes	235	105 (44.7)	130 (55.3)	11.3 (8.4, 18.2)	118	50 (42.4)	68 (57.6)	7.0 (4.4, 9.5)	0.6850 (0.4853, 0.9669) 0.0315	0.0299	
No	98	43 (43.9)	55 (56.1)	16.1 (9.8, 22.1)	48	20 (41.7)	28 (58.3)	11.4 (5.4, NE)	0.7119 (0.4133, 1.2264) 0.2208	0.2163	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Global Health Status

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Age										0.7419
<65	290	123 (42.4)	167 (57.6)	15.7 (9.8, 20.8)	136	53 (39.0)	83 (61.0)	8.4 (5.4, 11.4)	0.6744 (0.4846, 0.9385) 0.0195	0.0181
>=65	83	37 (44.6)	46 (55.4)	11.1 (5.9, 18.4)	48	24 (50.0)	24 (50.0)	7.5 (3.7, 13.6)	0.7581 (0.4504, 1.2759) 0.2971	0.2904

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Global Health Status

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8221
<75	359	154 (42.9)	205 (57.1)	14.4 (9.8, 18.4)	175	72 (41.1)	103 (58.9)	8.4 (5.9, 10.8)	0.6817 (0.5119, 0.9080) 0.0088	0.0080	
>=75	14	6 (42.9)	8 (57.1)	9.7 (4.2, NE)	9	5 (55.6)	4 (44.4)	9.9 (1.6, NE)	0.7418 (0.2255, 2.4400) 0.6230	0.6217	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Global Health Status

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.4526
White	176	67 (38.1)	109 (61.9)	18.6 (10.1, NE)	91	35 (38.5)	56 (61.5)	8.6 (4.2, 11.4)	0.6201 (0.4081, 0.9422) 0.0252	0.0237	
Non-White	197	93 (47.2)	104 (52.8)	11.3 (8.4, 18.0)	92	42 (45.7)	50 (54.3)	7.0 (5.8, 11.4)	0.7281 (0.5012, 1.0576) 0.0958	0.0917	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Global Health Status

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.5515
Asia	147	80 (54.4)	67 (45.6)	9.7 (7.2, 15.7)	66	32 (48.5)	34 (51.5)	6.5 (3.8, NE)	0.8101 (0.5333, 1.2304) 0.3233	0.3172	
North America	60	21 (35.0)	39 (65.0)	22.3 (6.3, NE)	33	13 (39.4)	20 (60.6)	8.6 (2.0, 11.4)	0.5603 (0.2735, 1.1477) 0.1133	0.1098	
Europe + Israel	166	59 (35.5)	107 (64.5)	18.6 (11.4, NE)	85	32 (37.6)	53 (62.4)	9.0 (4.5, 15.3)	0.5953 (0.3834, 0.9242) 0.0208	0.0191	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Global Health Status

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	200	94 (47.0)	106 (53.0)	13.1 (8.4, 18.4)	105	43 (41.0)	62 (59.0)	9.0 (5.3, 11.4)	0.7144 (0.4946, 1.0319)	0.0706	0.7522
1	173	66 (38.2)	107 (61.8)	16.1 (10.5, 22.3)	79	34 (43.0)	45 (57.0)	8.4 (4.5, 13.6)	0.6440 (0.4206, 0.9859)	0.0399	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Global Health Status

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.1501
0	60	25 (41.7)	35 (58.3)	9.7 (6.3, NE)	34	14 (41.2)	20 (58.8)	5.9 (4.5, 13.6)	0.6316 (0.3222, 1.2382) 0.1810	0.1759
1	108	43 (39.8)	65 (60.2)	16.3 (8.3, NE)	51	18 (35.3)	33 (64.7)	11.4 (9.0, NE)	1.0285 (0.5921, 1.7866) 0.9205	0.9212
2	115	45 (39.1)	70 (60.9)	22.3 (9.4, NE)	54	27 (50.0)	27 (50.0)	6.9 (2.9, 10.8)	0.4383 (0.2671, 0.7192) 0.0011	0.0008

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Global Health Status

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	47 (52.2)	43 (47.8)	11.4 (7.0, 18.4)	45	18 (40.0)	27 (60.0)	8.6 (3.1, NE)	0.7707 (0.4373, 1.3583) 0.3677	0.3642

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Global Health Status

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.6434
PD	174	62 (35.6)	112 (64.4)	18.0 (9.9, NE)	85	36 (42.4)	49 (57.6)	7.0 (5.3, 10.8)	0.5410 (0.3553, 0.8239) 0.0042	0.0036	
PR	48	25 (52.1)	23 (47.9)	11.3 (8.1, 22.3)	22	8 (36.4)	14 (63.6)	3.9 (3.1, NE)	0.7276 (0.3198, 1.6554) 0.4483	0.4390	
SD	82	38 (46.3)	44 (53.7)	14.4 (6.3, NE)	55	24 (43.6)	31 (56.4)	9.0 (4.5, 15.5)	0.7916 (0.4695, 1.3348) 0.3807	0.3754	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Global Health Status

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.7529
Yes	37	12 (32.4)	25 (67.6)	18.6 (8.8, NE)	15	3 (20.0)	12 (80.0)	NE (1.0, NE)	0.8346 (0.2281, 3.0531)	0.7846	
No	336	148 (44.0)	188 (56.0)	13.1 (9.7, 18.2)	169	74 (43.8)	95 (56.2)	8.4 (5.8, 9.9)	0.6897 (0.5184, 0.9175)	0.0099	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Global Health Status

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0052
Yes	24	12 (50.0)	12 (50.0)	9.9 (5.2, 18.6)	8	0	8 (100)	NE (NE, NE)	NE (NE, NE) 0.9942	0.1125	
No	349	148 (42.4)	201 (57.6)	14.4 (9.8, 18.4)	176	77 (43.8)	99 (56.3)	7.5 (5.4, 9.9)	0.6488 (0.4895, 0.8601) 0.0026	0.0023	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Global Health Status

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0990
Normal Function	202	73 (36.1)	129 (63.9)	20.8 (15.7, NE)	87	35 (40.2)	52 (59.8)	6.9 (4.2, 13.6)	0.5589 (0.3684, 0.8479) 0.0062	0.0052	
Mild Impairment	123	68 (55.3)	55 (44.7)	8.4 (6.0, 11.3)	69	30 (43.5)	39 (56.5)	9.0 (3.8, 11.4)	0.8168 (0.5262, 1.2677) 0.3669	0.3606	
Moderate Impairment	41	17 (41.5)	24 (58.5)	16.3 (6.3, NE)	23	9 (39.1)	14 (60.9)	11.4 (5.9, NE)	1.1662 (0.5192, 2.6194) 0.7097	0.7134	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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Global Health Status

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.8366
Normal Function	170	76 (44.7)	94 (55.3)	16.1 (9.6, 22.3)	98	42 (42.9)	56 (57.1)	8.4 (5.8, 11.4)	0.7138 (0.4856, 1.0491) 0.0862	0.0821
Mild Impairment	195	82 (42.1)	113 (57.9)	13.1 (8.8, 18.6)	84	34 (40.5)	50 (59.5)	8.6 (4.2, 10.8)	0.6618 (0.4396, 0.9963) 0.0479	0.0454

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline visceral disease										0.8300
Yes	332	141 (42.5)	191 (57.5)	14.4 (9.9, 18.6)	157	63 (40.1)	94 (59.9)	9.3 (6.5, 11.4)	0.7010 (0.5176, 0.9494) 0.0217	0.0206
No	41	19 (46.3)	22 (53.7)	9.8 (4.2, NE)	27	14 (51.9)	13 (48.1)	5.8 (2.3, 9.0)	0.6497 (0.3189, 1.3234) 0.2348	0.2288

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (IXRS)										0.6740
Positive	331	147 (44.4)	184 (55.6)	13.2 (9.8, 18.4)	163	68 (41.7)	95 (58.3)	8.6 (5.9, 11.4)	0.7072 (0.5273, 0.9484) 0.0207	0.0194
Negative	42	13 (31.0)	29 (69.0)	14.4 (8.4, NE)	21	9 (42.9)	12 (57.1)	5.8 (3.9, 9.9)	0.5127 (0.2103, 1.2502) 0.1419	0.1354

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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[c] Two-sided p-value from unstratified log-rank test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (derived)										0.9491
Positive	333	147 (44.1)	186 (55.9)	13.2 (9.8, 18.4)	166	70 (42.2)	96 (57.8)	8.4 (5.9, 11.4)	0.6964 (0.5206, 0.9315) 0.0148	0.0137
Negative	40	13 (32.5)	27 (67.5)	14.4 (8.4, NE)	18	7 (38.9)	11 (61.1)	9.9 (3.2, 9.9)	0.5972 (0.2295, 1.5542) 0.2908	0.2861

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.7716
HER2 IHC 1+	214	50 (23.4)	164 (76.6)	NE (21.5, NE)	107	30 (28.0)	77 (72.0)	10.2 (7.9, NE)	0.4908 (0.3068, 0.7852) 0.0030	0.0025	
HER2 IHC 2+/ISH Negative	159	40 (25.2)	119 (74.8)	NE (NE, NE)	77	27 (35.1)	50 (64.9)	10.1 (5.9, NE)	0.4416 (0.2688, 0.7256) 0.0013	0.0009	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.3198
1	221	52 (23.5)	169 (76.5)	NE (21.5, NE)	100	28 (28.0)	72 (72.0)	11.3 (8.4, 18.3)	0.5283 (0.3297, 0.8465) 0.0080	0.0070	
>=2	151	38 (25.2)	113 (74.8)	NE (18.7, NE)	83	29 (34.9)	54 (65.1)	8.4 (4.7, NE)	0.4073 (0.2471, 0.6712) 0.0004	0.0003	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]	
Prior CDK4/6										0.1369	
Yes	235	56 (23.8)	179 (76.2)	NE (21.5, NE)	118	32 (27.1)	86 (72.9)	10.2 (8.4, 18.3)	0.5198 (0.3322, 0.8133)	0.0036	
No	98	23 (23.5)	75 (76.5)	NE (18.7, NE)	48	21 (43.8)	27 (56.3)	7.5 (4.7, NE)	0.3029 (0.1652, 0.5553)	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age									0.8874
<65	290	74 (25.5)	216 (74.5) (21.5, NE)	136	43 (31.6)	93 (68.4) (6.5, 18.3)	0.4557 (0.3092, 0.6717) 0.0001	<0.0001	
>=65	83	16 (19.3)	67 (80.7) (18.7, NE)	48	14 (29.2)	34 (70.8) (7.5, NE)	0.4494 (0.2146, 0.9412) 0.0340	0.0298	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age									0.4591
<75	359	89 (24.8)	270 (75.2) (21.5, NE)	175	54 (30.9)	121 (69.1) (7.7, 18.3)	0.4620 (0.3259, 0.6550) <0.0001	<0.0001	
>=75	14	1 (7.1)	13 (92.9) (NE, NE)	9	3 (33.3)	6 (66.7) (1.4, NE)	0.2230 (0.0232, 2.1464) 0.1940	0.1545	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.9527
White	176	41 (23.3)	135 (76.7)	NE (21.5, NE)	91	26 (28.6)	65 (71.4)	10.1 (5.7, NE)	0.4947 (0.2983, 0.8203) 0.0064	0.0054	
Non-White	197	49 (24.9)	148 (75.1)	NE (18.7, NE)	92	31 (33.7)	61 (66.3)	11.3 (6.5, NE)	0.4399 (0.2769, 0.6989) 0.0005	0.0004	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.5872
Asia	147	41 (27.9)	106 (72.1)	NE (16.9, NE)	66	24 (36.4)	42 (63.6)	11.3 (6.3, NE)	0.4649 (0.2775, 0.7790) 0.0036	0.0029	
North America	60	8 (13.3)	52 (86.7)	NE (21.5, NE)	33	8 (24.2)	25 (75.8)	10.1 (4.4, NE)	0.3233 (0.1149, 0.9096) 0.0324	0.0247	
Europe + Israel	166	41 (24.7)	125 (75.3)	NE (18.7, NE)	85	25 (29.4)	60 (70.6)	10.2 (5.7, NE)	0.5209 (0.3127, 0.8676) 0.0122	0.0109	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	200	43 (21.5)	157 (78.5)	NE (NE, NE)	105	28 (26.7)	77 (73.3)	16.9 (7.7, NE)	0.4499 (0.2768, 0.7312)	0.0010	0.8566
1	173	47 (27.2)	126 (72.8)	21.5 (18.7, NE)	79	29 (36.7)	50 (63.3)	8.5 (6.1, 11.3)	0.4770 (0.2943, 0.7734)	0.0021	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1642
0	60	17 (28.3)	43 (71.7)	NE (10.9, NE)	34	9 (26.5)	25 (73.5)	NE (5.3, NE)	0.6659 (0.2919, 1.5192) 0.3339	0.3310	
1	108	30 (27.8)	78 (72.2)	NE (13.6, NE)	51	16 (31.4)	35 (68.6)	16.9 (8.5, NE)	0.6627 (0.3584, 1.2256) 0.1897	0.1870	
2	115	26 (22.6)	89 (77.4)	NE (21.5, NE)	54	15 (27.8)	39 (72.2)	8.4 (6.3, NE)	0.3983 (0.2021, 0.7850) 0.0078	0.0060	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	17 (18.9)	73 (81.1)	NE (NE, NE)	45	17 (37.8)	28 (62.2)	8.4 (5.8, 18.3)	0.2872 (0.1429, 0.5774) 0.0005	0.0002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.9495
PD	174	38 (21.8)	136 (78.2)	NE (18.7, NE)	85	23 (27.1)	62 (72.9)	NE (5.9, NE)	0.4472 (0.2609, 0.7665) 0.0034	0.0027	
PR	48	17 (35.4)	31 (64.6)	21.5 (11.2, NE)	22	7 (31.8)	15 (68.2)	NE (3.1, NE)	0.5388 (0.2155, 1.3469) 0.1859	0.1775	
SD	82	18 (22.0)	64 (78.0)	NE (NE, NE)	55	18 (32.7)	37 (67.3)	11.3 (8.4, NE)	0.4690 (0.2404, 0.9149) 0.0264	0.0231	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.5949
Yes	37	10 (27.0)	27 (73.0)	NE (8.4, NE)	15	3 (20.0)	12 (80.0)	NE (1.0, NE)	0.7093 (0.1907, 2.6385) 0.6083	0.6090
No	336	80 (23.8)	256 (76.2)	NE (21.5, NE)	169	54 (32.0)	115 (68.0)	10.2 (7.9, 18.3)	0.4434 (0.3106, 0.6331) <0.0001	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.2132
Yes	24	7 (29.2)	17 (70.8)	NE (5.4, NE)	8	1 (12.5)	7 (87.5)	NE (0.7, NE)	1.4754 (0.1786, 12.1866) 0.7181	0.7093
No	349	83 (23.8)	266 (76.2)	NE (21.5, NE)	176	56 (31.8)	120 (68.2)	10.2 (7.7, 18.3)	0.4390 (0.3095, 0.6227) <0.0001	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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## Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0201
Normal Function	202	41 (20.3)	161 (79.7)	NE (21.5, NE)	87	29 (33.3)	58 (66.7)	8.5 (5.3, NE)	0.3137 (0.1908, 0.5156) <0.0001	<0.0001	
Mild Impairment	123	35 (28.5)	88 (71.5)	NE (16.3, NE)	69	22 (31.9)	47 (68.1)	8.4 (6.1, 16.9)	0.5095 (0.2932, 0.8855) 0.0168	0.0149	
Moderate Impairment	41	12 (29.3)	29 (70.7)	18.7 (13.6, NE)	23	4 (17.4)	19 (82.6)	NE (11.3, NE)	1.5179 (0.4819, 4.7813) 0.4759	0.4725	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.4238
Normal Function	170	40 (23.5)	130 (76.5)	NE (21.5, NE)	98	34 (34.7)	64 (65.3)	18.3 (6.1, NE)	0.4115 (0.2573, 0.6579) 0.0002	0.0001
Mild Impairment	195	49 (25.1)	146 (74.9)	NE (18.7, NE)	84	23 (27.4)	61 (72.6)	10.1 (6.5, 16.9)	0.5096 (0.3048, 0.8518) 0.0101	0.0088

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.0561
Yes	332	81 (24.4)	251 (75.6)	NE (21.5, NE)	157	45 (28.7)	112 (71.3)	11.3 (8.4, NE)	0.5360 (0.3692, 0.7781) 0.0010	0.0009	
No	41	9 (22.0)	32 (78.0)	NE (NE, NE)	27	12 (44.4)	15 (55.6)	5.3 (4.3, NE)	0.1887 (0.0724, 0.4923) 0.0007	0.0002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.3838
Positive	331	78 (23.6)	253 (76.4)	NE (21.5, NE)	163	51 (31.3)	112 (68.7)	10.2 (7.9, NE)	0.4332 (0.3013, 0.6228)	<0.0001	
Negative	42	12 (28.6)	30 (71.4)	NE (10.9, NE)	21	6 (28.6)	15 (71.4)	NE (4.5, NE)	0.8382 (0.3088, 2.2753)	0.7221	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (derived)										0.1757
Positive	333	78 (23.4)	255 (76.6)	NE (21.5, NE)	166	53 (31.9)	113 (68.1)	10.2 (7.9, 18.3)	0.4223 (0.2949, 0.6048) <0.0001	<0.0001
Negative	40	12 (30.0)	28 (70.0)	NE (5.4, NE)	18	4 (22.2)	14 (77.8)	NE (4.5, NE)	1.1032 (0.3505, 3.4728) 0.8666	0.8693

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.9633
HER2 IHC 1+	214	94 (43.9)	120 (56.1)	11.3 (8.3, 21.5)	107	49 (45.8)	58 (54.2)	4.7 (4.2, 7.2)	0.5449 (0.3814, 0.7784) 0.0008	0.0007
HER2 IHC 2+/ISH Negative	159	65 (40.9)	94 (59.1)	16.8 (9.0, NE)	77	37 (48.1)	40 (51.9)	6.1 (2.9, 10.5)	0.5728 (0.3801, 0.8631) 0.0077	0.0068

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.6146
1	221	98 (44.3)	123 (55.7)	11.3 (7.2, 21.7)	100	48 (48.0)	52 (52.0)	5.8 (3.8, 7.7)	0.6082 (0.4287, 0.8629) 0.0053	0.0048	
>=2	151	61 (40.4)	90 (59.6)	16.6 (10.4, 27.2)	83	38 (45.8)	45 (54.2)	4.7 (2.9, 8.4)	0.5092 (0.3347, 0.7747) 0.0016	0.0013	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.2241
Yes	235	98 (41.7)	137 (58.3)	16.4 (8.5, 23.0)	118	54 (45.8)	64 (54.2)	5.8 (3.7, 7.7)	0.5871 (0.4188, 0.8231) 0.0020	0.0017	
No	98	42 (42.9)	56 (57.1)	16.6 (10.4, NE)	48	27 (56.3)	21 (43.8)	4.3 (1.7, 8.4)	0.3722 (0.2255, 0.6144) 0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1712
<65	290	115 (39.7)	175 (60.3)	16.8 (11.3, 23.0)	136	62 (45.6)	74 (54.4)	5.8 (3.8, 7.7)	0.5069 (0.3693, 0.6958) <0.0001	<0.0001	
>=65	83	44 (53.0)	39 (47.0)	7.1 (4.4, 16.6)	48	24 (50.0)	24 (50.0)	4.8 (2.9, 10.5)	0.7916 (0.4779, 1.3114) 0.3643	0.3604	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2154
<75	359	152 (42.3)	207 (57.7)	16.4 (10.0, 21.5)	175	82 (46.9)	93 (53.1)	4.8 (4.2, 7.2)	0.5388 (0.4092, 0.7095) <0.0001	<0.0001	
>=75	14	7 (50.0)	7 (50.0)	9.7 (2.1, NE)	9	4 (44.4)	5 (55.6)	NE (0.8, NE)	1.2098 (0.3523, 4.1542) 0.7622	0.7726	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.2865
White	176	74 (42.0)	102 (58.0)	16.0 (8.5, 21.5)	91	37 (40.7)	54 (59.3)	6.7 (4.4, NE)	0.6895 (0.4613, 1.0308) 0.0699	0.0671	
Non-White	197	85 (43.1)	112 (56.9)	16.6 (8.7, 27.2)	92	49 (53.3)	43 (46.7)	4.7 (2.9, 7.1)	0.4730 (0.3299, 0.6783) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.5273
Asia	147	71 (48.3)	76 (51.7)	11.3 (7.5, 23.0)	66	38 (57.6)	28 (42.4)	4.7 (2.9, 7.0)	0.5005 (0.3347, 0.7486) 0.0008	0.0006	
North America	60	18 (30.0)	42 (70.0)	16.8 (7.3, NE)	33	13 (39.4)	20 (60.6)	4.5 (1.5, NE)	0.4281 (0.2014, 0.9098) 0.0274	0.0227	
Europe + Israel	166	70 (42.2)	96 (57.8)	16.0 (8.5, NE)	85	35 (41.2)	50 (58.8)	7.2 (4.4, NE)	0.7009 (0.4643, 1.0581) 0.0908	0.0883	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											
0	200	78 (39.0)	122 (61.0)	21.7 (12.0, NE)	105	48 (45.7)	57 (54.3)	4.7 (2.1, 8.4)	0.4736 (0.3278, 0.6841) 0.0001	<0.0001	0.1495
1	173	81 (46.8)	92 (53.2)	9.0 (6.7, 16.6)	79	38 (48.1)	41 (51.9)	6.1 (4.4, 8.4)	0.6724 (0.4527, 0.9986) 0.0492	0.0466	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.2965
0	60	30 (50.0)	30 (50.0)	9.7 (5.1, 17.6)	34	13 (38.2)	21 (61.8)	5.9 (2.9, NE)	0.7739 (0.3939, 1.5205) 0.4569	0.4546	
1	108	42 (38.9)	66 (61.1)	13.1 (9.6, 27.2)	51	21 (41.2)	30 (58.8)	7.2 (1.6, NE)	0.6629 (0.3906, 1.1251) 0.1277	0.1255	
2	115	40 (34.8)	75 (65.2)	21.5 (21.5, NE)	54	26 (48.1)	28 (51.9)	4.6 (2.1, 8.4)	0.4021 (0.2409, 0.6712) 0.0005	0.0003	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	47 (52.2)	43 (47.8)	8.3 (6.0, 16.4)	45	26 (57.8)	19 (42.2)	4.2 (1.5, 7.7)	0.5275 (0.3218, 0.8647) 0.0112	0.0099	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.8344
PD	174	63 (36.2)	111 (63.8)	27.2 (8.5, NE)	85	34 (40.0)	51 (60.0)	7.0 (3.7, NE)	0.6111 (0.4000, 0.9336) 0.0227	0.0213
PR	48	25 (52.1)	23 (47.9)	11.3 (7.0, 21.5)	22	9 (40.9)	13 (59.1)	8.4 (0.9, NE)	0.6322 (0.2880, 1.3876) 0.2529	0.2443
SD	82	37 (45.1)	45 (54.9)	16.6 (8.3, NE)	55	28 (50.9)	27 (49.1)	4.7 (3.8, 7.2)	0.5554 (0.3355, 0.9195) 0.0222	0.0205

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.7007
Yes	37	13 (35.1)	24 (64.9)	16.6 (6.7, NE)	15	4 (26.7)	11 (73.3)	NE (1.0, NE)	0.7945 (0.2539, 2.4864) 0.6927	0.6910	
No	336	146 (43.5)	190 (56.5)	13.1 (9.6, 21.5)	169	82 (48.5)	87 (51.5)	4.8 (4.2, 7.2)	0.5555 (0.4212, 0.7325) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0998
Yes	24	10 (41.7)	14 (58.3)	16.6 (4.9, NE)	8	1 (12.5)	7 (87.5)	NE (0.7, NE)	2.4679 (0.3113, 19.5677) 0.3925	0.3730	
No	349	149 (42.7)	200 (57.3)	16.0 (9.8, 21.5)	176	85 (48.3)	91 (51.7)	4.8 (3.8, 7.1)	0.5419 (0.4125, 0.7118) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0098
Normal Function	202	76 (37.6)	126 (62.4)	16.6 (12.0, NE)	87	42 (48.3)	45 (51.7)	4.3 (1.5, 8.6)	0.4147 (0.2811, 0.6120) <0.0001	<0.0001	
Mild Impairment	123	59 (48.0)	64 (52.0)	9.7 (6.7, 23.0)	69	33 (47.8)	36 (52.2)	5.8 (4.2, 8.4)	0.6300 (0.4062, 0.9772) 0.0391	0.0368	
Moderate Impairment	41	22 (53.7)	19 (46.3)	7.0 (2.8, NE)	23	8 (34.8)	15 (65.2)	NE (4.5, NE)	1.5143 (0.6732, 3.4064) 0.3157	0.3096	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.6312
Normal Function	170	79 (46.5)	91 (53.5)	16.0 (7.7, 21.5)	98	47 (48.0)	51 (52.0)	5.9 (3.7, 8.6)	0.6123 (0.4241, 0.8840) 0.0088	0.0079	
Mild Impairment	195	78 (40.0)	117 (60.0)	16.6 (8.7, 23.0)	84	38 (45.2)	46 (54.8)	4.8 (2.9, 8.4)	0.5175 (0.3472, 0.7712) 0.0012	0.0010	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.7371
Yes	332	140 (42.2)	192 (57.8)	16.0 (9.8, 21.5)	157	75 (47.8)	82 (52.2)	4.8 (3.8, 7.7)	0.5503 (0.4134, 0.7324) <0.0001	<0.0001	
No	41	19 (46.3)	22 (53.7)	11.3 (5.1, NE)	27	11 (40.7)	16 (59.3)	5.9 (1.7, NE)	0.6754 (0.3130, 1.4575) 0.3173	0.3078	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.1966
Positive	331	138 (41.7)	193 (58.3)	16.4 (10.4, 21.7)	163	77 (47.2)	86 (52.8)	5.8 (4.2, 7.7)	0.5247 (0.3946, 0.6978)	<0.0001	
Negative	42	21 (50.0)	21 (50.0)	6.0 (2.9, 17.6)	21	9 (42.9)	12 (57.1)	5.9 (1.5, NE)	0.9633 (0.4334, 2.1410)	0.9223	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.0241
Positive	333	139 (41.7)	194 (58.3)	16.4 (10.0, 21.7)	166	81 (48.8)	85 (51.2)	4.7 (3.7, 7.1)	0.5074 (0.3834, 0.6715) <0.0001	<0.0001	
Negative	40	20 (50.0)	20 (50.0)	6.0 (2.9, 17.6)	18	5 (27.8)	13 (72.2)	NE (3.4, NE)	1.5391 (0.5688, 4.1648) 0.3959	0.3951	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.8526
HER2 IHC 1+	214	73 (34.1)	141 (65.9)	19.2 (13.6, NE)	107	28 (26.2)	79 (73.8)	11.1 (7.1, NE)	0.7465 (0.4748, 1.1738)	0.2027
HER2 IHC 2+/ISH Negative	159	47 (29.6)	112 (70.4)	21.7 (18.7, NE)	77	20 (26.0)	57 (74.0)	NE (7.5, NE)	0.7650 (0.4497, 1.3016)	0.3220

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.2620
1	221	77 (34.8)	144 (65.2)	21.7 (16.3, NE)	100	26 (26.0)	74 (74.0)	11.1 (7.7, NE)	0.9245 (0.5876, 1.4545)	0.7312 0.7341
>=2	151	43 (28.5)	108 (71.5)	NE (16.6, NE)	83	22 (26.5)	61 (73.5)	11.7 (6.9, NE)	0.5636 (0.3306, 0.9608)	0.0331 0.0351

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6									0.1997
Yes	235	74 (31.5)	161 (68.5) (16.7, NE)	118	24 (20.3)	94 (79.7) (10.2, NE)	0.9437 (0.5890, 1.5119) 0.8095	0.8073	
No	98	35 (35.7)	63 (64.3) (13.1, NE)	48	18 (37.5)	30 (62.5) (6.1, NE)	0.5963 (0.3336, 1.0657) 0.0809	0.0775	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4613
<65	290	94 (32.4)	196 (67.6)	22.3 (19.2, NE)	136	32 (23.5)	104 (76.5)	NE (7.1, NE)	0.8342 (0.5530, 1.2582) 0.3872	0.3841	
>=65	83	26 (31.3)	57 (68.7)	17.0 (13.8, NE)	48	16 (33.3)	32 (66.7)	11.1 (7.5, NE)	0.5850 (0.3055, 1.1204) 0.1058	0.1023	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5378
<75	359	116 (32.3)	243 (67.7)	21.7 (17.0, NE)	175	46 (26.3)	129 (73.7)	11.7 (7.7, NE)	0.7485 (0.5271, 1.0627) 0.1053	0.1032	
>=75	14	4 (28.6)	10 (71.4)	16.7 (8.5, NE)	9	2 (22.2)	7 (77.8)	NE (3.7, NE)	1.0547 (0.1756, 6.3355) 0.9536	0.9533	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Race										0.6615
White	176	54 (30.7)	122 (69.3)	21.7 (16.7, NE)	91	20 (22.0)	71 (78.0)	11.1 (8.4, NE)	0.8197 (0.4824, 1.3928) 0.4622	0.4630
Non-White	197	66 (33.5)	131 (66.5)	22.8 (16.3, NE)	92	28 (30.4)	64 (69.6)	11.7 (6.9, NE)	0.7123 (0.4533, 1.1190) 0.1410	0.1395

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.8646
Asia	147	51 (34.7)	96 (65.3)	22.8 (13.6, NE)	66	19 (28.8)	47 (71.2)	NE (6.9, NE)	0.7913 (0.4626, 1.3536) 0.3928	0.3928	
North America	60	15 (25.0)	45 (75.0)	22.3 (19.2, NE)	33	7 (21.2)	26 (78.8)	NE (4.4, NE)	0.7107 (0.2779, 1.8178) 0.4761	0.4741	
Europe + Israel	166	54 (32.5)	112 (67.5)	21.7 (13.8, NE)	85	22 (25.9)	63 (74.1)	11.1 (8.4, NE)	0.7726 (0.4646, 1.2848) 0.3202	0.3192	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	200	65 (32.5)	135 (67.5)	22.8 (16.7, NE)	105	24 (22.9)	81 (77.1)	NE (11.1, NE)	0.8145 (0.5054, 1.3128) 0.3996	0.3993	0.7390
1	173	55 (31.8)	118 (68.2)	18.7 (13.6, NE)	79	24 (30.4)	55 (69.6)	10.2 (6.9, NE)	0.6979 (0.4237, 1.1496) 0.1578	0.1542	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.0651
0	60	19 (31.7)	41 (68.3)	18.7 (10.4, 18.7)	34	9 (26.5)	25 (73.5)	7.1 (5.3, NE)	0.7737 (0.3433, 1.7437) 0.5360	0.5385	
1	108	39 (36.1)	69 (63.9)	17.0 (11.1, 22.8)	51	12 (23.5)	39 (76.5)	NE (10.2, NE)	1.2270 (0.6376, 2.3613) 0.5402	0.5376	
2	115	37 (32.2)	78 (67.8)	22.3 (16.7, NE)	54	20 (37.0)	34 (63.0)	7.5 (4.4, 11.7)	0.4344 (0.2424, 0.7786) 0.0051	0.0040	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	25 (27.8)	65 (72.2)	NE (16.3, NE)	45	7 (15.6)	38 (84.4)	NE (NE, NE)	1.1060 (0.4709, 2.5975) 0.8171	0.8159

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.7517
PD	174	52 (29.9)	122 (70.1)	22.8 (16.3, NE)	85	23 (27.1)	62 (72.9)	NE (6.9, NE)	0.6489 (0.3905, 1.0781) 0.0950	0.0920	
PR	48	16 (33.3)	32 (66.7)	22.3 (11.2, NE)	22	4 (18.2)	18 (81.8)	11.7 (11.7, NE)	0.9784 (0.3178, 3.0119) 0.9696	0.9766	
SD	82	25 (30.5)	57 (69.5)	19.2 (12.0, NE)	55	15 (27.3)	40 (72.7)	11.1 (8.4, NE)	0.7585 (0.3944, 1.4587) 0.4074	0.4061	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.9955
Yes	37	12 (32.4)	25 (67.6)	18.7 (9.7, NE)	15	3 (20.0)	12 (80.0)	NE (5.9, NE)	0.6381 (0.1693, 2.4054) 0.5070	0.5036	
No	336	108 (32.1)	228 (67.9)	22.3 (16.7, NE)	169	45 (26.6)	124 (73.4)	11.7 (8.4, NE)	0.7692 (0.5384, 1.0988) 0.1492	0.1467	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.2127
Yes	24	9 (37.5)	15 (62.5)	18.7 (7.1, NE)	8	1 (12.5)	7 (87.5)	NE (5.9, NE)	2.0152 (0.2486, 16.3377) 0.5117	0.5032
No	349	111 (31.8)	238 (68.2)	21.7 (16.7, NE)	176	47 (26.7)	129 (73.3)	11.7 (8.4, NE)	0.7275 (0.5124, 1.0327) 0.0751	0.0734

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Renal function at baseline										0.0703
Normal Function	202	70 (34.7)	132 (65.3)	21.7 (13.6, NE)	87	18 (20.7)	69 (79.3)	NE (6.9, NE)	1.0839 (0.6399, 1.8359) 0.7645	0.7664
Mild Impairment	123	35 (28.5)	88 (71.5)	22.8 (16.3, NE)	69	23 (33.3)	46 (66.7)	8.4 (6.1, 11.7)	0.4224 (0.2411, 0.7400) 0.0026	0.0019
Moderate Impairment	41	15 (36.6)	26 (63.4)	16.7 (11.2, NE)	23	7 (30.4)	16 (69.6)	NE (7.7, NE)	1.0453 (0.4245, 2.5740) 0.9232	0.9226

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline									0.0853
Normal Function	170	56 (32.9)	114 (67.1) (17.0, NE)	98	33 (33.7)	65 (66.3) (6.9, NE)	0.5949 (0.3821, 0.9265) 0.0216	0.0201	
Mild Impairment	195	64 (32.8)	131 (67.2) (13.1, NE)	84	15 (17.9)	69 (82.1) (10.2, NE)	1.1061 (0.6232, 1.9632) 0.7306	0.7315	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline visceral disease										0.0435
Yes	332	108 (32.5)	224 (67.5)	21.7 (16.6, NE)	157	37 (23.6)	120 (76.4)	NE (10.2, NE)	0.8725 (0.5961, 1.2770) 0.4828	0.4816
No	41	12 (29.3)	29 (70.7)	NE (13.6, NE)	27	11 (40.7)	16 (59.3)	5.7 (3.7, NE)	0.4089 (0.1701, 0.9831) 0.0457	0.0393

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.3344
Positive	331	109 (32.9)	222 (67.1)	21.7 (16.7, NE)	163	41 (25.2)	122 (74.8)	11.7 (8.4, NE)	0.8049 (0.5575, 1.1622) 0.2469	0.2444	
Negative	42	11 (26.2)	31 (73.8)	18.7 (12.5, NE)	21	7 (33.3)	14 (66.7)	NE (3.4, NE)	0.5484 (0.2019, 1.4895) 0.2386	0.2323	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.5290
Positive	333	108 (32.4)	225 (67.6)	21.7 (16.7, NE)	166	42 (25.3)	124 (74.7)	11.7 (8.4, NE)	0.7830 (0.5435, 1.1279) 0.1890	0.1866	
Negative	40	12 (30.0)	28 (70.0)	18.7 (8.5, NE)	18	6 (33.3)	12 (66.7)	NE (3.0, NE)	0.6357 (0.2294, 1.7617) 0.3837	0.3785	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.5104
HER2 IHC 1+	214	86 (40.2)	128 (59.8)	17.0 (9.9, 21.4)	107	48 (44.9)	59 (55.1)	6.9 (4.4, 9.1)	0.5615 (0.3904, 0.8077) 0.0019	0.0016	
HER2 IHC 2+/ISH Negative	159	71 (44.7)	88 (55.3)	13.1 (9.2, 18.7)	77	34 (44.2)	43 (55.8)	8.5 (4.2, 16.2)	0.6996 (0.4624, 1.0584) 0.0908	0.0880	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	
Number of prior lines of chemotherapy in a metastatic setting									0.4704
1	221	96 (43.4)	125 (56.6)	12.7 (8.8, 17.3)	100	46 (46.0)	54 (54.0)	7.9 (4.2, 11.3) 0.6829 (0.4779, 0.9760) 0.0363	0.0348
>=2	151	61 (40.4)	90 (59.6)	16.0 (9.9, 21.4)	83	36 (43.4)	47 (56.6)	6.1 (4.4, 8.6) 0.5176 (0.3381, 0.7924) 0.0024	0.0021

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Prior CDK4/6										0.4976
Yes	235	95 (40.4)	140 (59.6)	13.6 (10.1, 17.3)	118	53 (44.9)	65 (55.1)	6.0 (4.2, 8.6)	0.5675 (0.4025, 0.8003) 0.0012	0.0010
No	98	46 (46.9)	52 (53.1)	16.0 (7.5, NE)	48	21 (43.8)	27 (56.3)	11.1 (4.2, 16.2)	0.7389 (0.4377, 1.2474) 0.2574	0.2561

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Age										0.9204
<65	290	123 (42.4)	167 (57.6)	13.1 (9.9, 21.4)	136	59 (43.4)	77 (56.6)	6.5 (4.4, 8.6)	0.6035 (0.4392, 0.8293) 0.0018	0.0016
>=65	83	34 (41.0)	49 (59.0)	13.8 (8.3, NE)	48	23 (47.9)	25 (52.1)	9.1 (3.1, 11.7)	0.6009 (0.3489, 1.0352) 0.0664	0.0654

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5396
<75	359	151 (42.1)	208 (57.9)	13.6 (10.4, 17.6)	175	77 (44.0)	98 (56.0)	6.5 (4.4, 9.0)	0.6047 (0.4567, 0.8005) 0.0004	0.0004	
>=75	14	6 (42.9)	8 (57.1)	14.1 (2.9, NE)	9	5 (55.6)	4 (44.4)	11.1 (2.8, NE)	0.6927 (0.1979, 2.4240) 0.5656	0.5635	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race									0.3360
White	176	69 (39.2)	107 (60.8)	91	40 (44.0)	51 (56.0)	6.9 (3.9, 11.1)	0.5115 (0.3427, 0.7634)	0.0008
Non-White	197	88 (44.7)	109 (55.3)	92	42 (45.7)	50 (54.3)	8.5 (5.8, 9.1)	0.7097 (0.4885, 1.0310)	0.0699

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]	
Region										0.2376	
Asia	147	74 (50.3)	73 (49.7)	11.8 (7.0, 17.5)	66	34 (51.5)	32 (48.5)	6.5 (5.8, 9.1)	0.7150 (0.4738, 1.0788)	0.1084	
North America	60	21 (35.0)	39 (65.0)	11.2 (7.1, NE)	33	7 (21.2)	26 (78.8)	7.9 (4.4, NE)	0.9792 (0.4046, 2.3703)	0.9613	
Europe + Israel	166	62 (37.3)	104 (62.7)	16.0 (11.8, NE)	85	41 (48.2)	44 (51.8)	5.4 (3.2, 11.1)	0.4819 (0.3215, 0.7225)	0.0003	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
ECOG PS										0.6458
0	200	85 (42.5)	115 (57.5)	16.7 (11.8, 18.7)	105	43 (41.0)	62 (59.0)	7.9 (5.8, 11.7)	0.6466 (0.4455, 0.9384) 0.0218	0.0208
1	173	72 (41.6)	101 (58.4)	11.3 (8.8, 22.3)	79	39 (49.4)	40 (50.6)	6.1 (4.2, 8.6)	0.5715 (0.3821, 0.8549) 0.0065	0.0058

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.7158
0	60	30 (50.0)	30 (50.0)	8.8 (3.9, 17.6)	34	16 (47.1)	18 (52.9)	5.9 (3.1, 16.2)	0.6758 (0.3621, 1.2614) 0.2185	0.2161
1	108	43 (39.8)	65 (60.2)	13.1 (7.6, NE)	51	23 (45.1)	28 (54.9)	9.0 (4.3, 17.1)	0.7516 (0.4520, 1.2498) 0.2711	0.2681
2	115	48 (41.7)	67 (58.3)	16.7 (11.8, 22.3)	54	22 (40.7)	32 (59.3)	7.9 (3.5, 11.7)	0.4746 (0.2755, 0.8178) 0.0073	0.0059

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	36 (40.0)	54 (60.0)	21.4 (7.1, NE)	45	21 (46.7)	24 (53.3)	6.5 (3.2, 9.1)	0.5854 (0.3391, 1.0106) 0.0546	0.0517

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.1580
PD	174	69 (39.7)	105 (60.3)	13.6 (9.2, 18.7)	85	33 (38.8)	52 (61.2)	6.9 (4.2, NE)	0.6350 (0.4144, 0.9730) 0.0370	0.0353	
PR	48	20 (41.7)	28 (58.3)	22.3 (5.7, NE)	22	14 (63.6)	8 (36.4)	3.9 (2.8, 9.0)	0.3486 (0.1723, 0.7053) 0.0034	0.0021	
SD	82	41 (50.0)	41 (50.0)	9.2 (6.9, 17.6)	55	26 (47.3)	29 (52.7)	9.0 (5.4, 16.2)	0.8188 (0.4972, 1.3485) 0.4323	0.4351	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Reported history of CNS metastases										0.4675
Yes	37	15 (40.5)	22 (59.5)	11.8 (7.1, NE)	15	4 (26.7)	11 (73.3)	8.5 (6.0, 17.1)	0.8570 (0.2790, 2.6321)	0.7873
No	336	142 (42.3)	194 (57.7)	13.8 (10.4, 17.5)	169	78 (46.2)	91 (53.8)	6.5 (4.4, 9.0)	0.6025 (0.4544, 0.7990)	0.0004

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.0981
Yes	24	13 (54.2)	11 (45.8)	8.8 (4.2, NE)	8	2 (25.0)	6 (75.0)	12.8 (8.5, 17.1)	1.6826 (0.3736, 7.5782) 0.4980	0.4933
No	349	144 (41.3)	205 (58.7)	14.1 (11.3, 17.6)	176	80 (45.5)	96 (54.5)	6.5 (4.4, 9.0)	0.5850 (0.4425, 0.7735) 0.0002	0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%) Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%) Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline									0.2373
Normal Function	202	80 (39.6)	122 (60.4) 22.3 (10.1, NE)	87	40 (46.0)	47 (54.0) 5.3 (3.5, 16.2)	0.5465 (0.3710, 0.8051) 0.0022	0.0019	
Mild Impairment	123	58 (47.2)	65 (52.8) 13.1 (7.1, 17.3)	69	32 (46.4)	37 (53.6) 6.5 (4.2, 9.0)	0.5473 (0.3474, 0.8623) 0.0094	0.0085	
Moderate Impairment	41	18 (43.9)	23 (56.1) 16.7 (5.6, NE)	23	9 (39.1)	14 (60.9) 17.1 (5.9, NE)	1.0308 (0.4586, 2.3168) 0.9415	0.9423	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Hepatic function at baseline										0.9916
Normal Function	170	72 (42.4)	98 (57.6)	16.0 (10.1, NE)	98	45 (45.9)	53 (54.1)	8.5 (5.8, 11.1)	0.5949 (0.4072, 0.8692) 0.0073	0.0067
Mild Impairment	195	84 (43.1)	111 (56.9)	12.5 (9.2, 17.6)	84	37 (44.0)	47 (56.0)	6.0 (3.5, 11.3)	0.6101 (0.4099, 0.9081) 0.0149	0.0137

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Baseline visceral disease										0.2324
Yes	332	140 (42.2)	192 (57.8)	13.6 (9.9, 17.6)	157	67 (42.7)	90 (57.3)	7.9 (5.8, 11.1)	0.6547 (0.4869, 0.8805) 0.0051	0.0048
No	41	17 (41.5)	24 (58.5)	16.7 (5.7, NE)	27	15 (55.6)	12 (44.4)	4.4 (2.8, 9.0)	0.4040 (0.1930, 0.8458) 0.0162	0.0129

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (IXRS)										0.9708
Positive	331	138 (41.7)	193 (58.3)	13.8 (11.2, 17.5)	163	71 (43.6)	92 (56.4)	7.9 (5.4, 11.1)	0.6148 (0.4593, 0.8229) 0.0011	0.0010
Negative	42	19 (45.2)	23 (54.8)	8.8 (2.9, NE)	21	11 (52.4)	10 (47.6)	5.3 (3.9, 9.0)	0.6246 (0.2865, 1.3615) 0.2365	0.2328

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.8648
Positive	333	140 (42.0)	193 (58.0)	13.8 (10.8, 17.5)	166	74 (44.6)	92 (55.4)	7.7 (4.4, 9.1)	0.6107 (0.4583, 0.8138) 0.0008	0.0007	
Negative	40	17 (42.5)	23 (57.5)	11.8 (2.9, NE)	18	8 (44.4)	10 (55.6)	5.9 (4.4, 9.0)	0.6330 (0.2633, 1.5220) 0.3070	0.3006	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.1614
HER2 IHC 1+	214	91 (42.5)	123 (57.5)	12.8 (10.4, 21.5)	107	56 (52.3)	51 (47.7)	5.4 (3.5, 7.9)	0.4665 (0.3292, 0.6611) <0.0001	<0.0001	
HER2 IHC 2+/ISH Negative	159	65 (40.9)	94 (59.1)	14.3 (12.5, 21.7)	77	32 (41.6)	45 (58.4)	6.1 (4.6, NE)	0.7361 (0.4792, 1.1308) 0.1619	0.1554	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.1727
1	221	102 (46.2)	119 (53.8)	12.7 (8.3, 15.2)	100	48 (48.0)	52 (52.0)	6.0 (4.2, 9.7)	0.6830 (0.4818, 0.9683) 0.0323	0.0312	
>=2	151	54 (35.8)	97 (64.2)	17.5 (12.5, 23.0)	83	40 (48.2)	43 (51.8)	5.9 (4.4, 8.5)	0.4256 (0.2770, 0.6538) 0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.7051
Yes	235	94 (40.0)	141 (60.0)	13.6 (10.8, 21.5)	118	56 (47.5)	62 (52.5)	5.8 (4.3, 8.5)	0.5543 (0.3953, 0.7774) 0.0006	0.0005	
No	98	49 (50.0)	49 (50.0)	13.8 (9.1, 21.7)	48	23 (47.9)	25 (52.1)	7.1 (4.2, 9.7)	0.6218 (0.3716, 1.0404) 0.0704	0.0679	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Age										0.0594
<65	290	118 (40.7)	172 (59.3)	14.6 (12.5, 21.5)	136	67 (49.3)	69 (50.7)	5.3 (4.2, 6.2)	0.4966 (0.3648, 0.6762)	<0.0001
>=65	83	38 (45.8)	45 (54.2)	10.8 (5.9, 19.3)	48	21 (43.8)	27 (56.3)	9.7 (4.7, 18.5)	0.8481 (0.4894, 1.4695)	0.5516

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0349
<75	359	150 (41.8)	209 (58.2)	13.8 (11.3, 19.3)	175	86 (49.1)	89 (50.9)	5.4 (4.4, 7.0)	0.5309 (0.4038, 0.6979) <0.0001	<0.0001	
>=75	14	6 (42.9)	8 (57.1)	10.8 (2.8, NE)	9	2 (22.2)	7 (77.8)	11.3 (9.7, NE)	2.6548 (0.5324, 13.2387) 0.2337	0.2158	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.3539
White	176	71 (40.3)	105 (59.7)	13.6 (11.1, 21.7)	91	45 (49.5)	46 (50.5)	5.3 (2.8, 7.9)	0.5125 (0.3485, 0.7535) 0.0007	0.0005	
Non-White	197	85 (43.1)	112 (56.9)	13.1 (10.0, 19.3)	92	43 (46.7)	49 (53.3)	6.1 (4.6, 9.7)	0.6129 (0.4204, 0.8934) 0.0109	0.0099	

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[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.5462
Asia	147	70 (47.6)	77 (52.4)	13.1 (9.2, 19.3)	66	32 (48.5)	34 (51.5)	7.0 (4.6, 11.3)	0.6466 (0.4215, 0.9918) 0.0458	0.0432	
North America	60	20 (33.3)	40 (66.7)	14.6 (10.4, NE)	33	13 (39.4)	20 (60.6)	5.8 (2.0, NE)	0.5465 (0.2611, 1.1440) 0.1089	0.1028	
Europe + Israel	166	66 (39.8)	100 (60.2)	13.6 (11.1, 23.0)	85	43 (50.6)	42 (49.4)	5.3 (2.9, 9.7)	0.5096 (0.3432, 0.7567) 0.0008	0.0006	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.3522
0	200	80 (40.0)	120 (60.0)	18.2 (12.5, 21.7)	105	49 (46.7)	56 (53.3)	5.4 (3.8, 9.7)	0.5040 (0.3498, 0.7262) 0.0002	0.0002	
1	173	76 (43.9)	97 (56.1)	12.8 (9.0, 14.6)	79	39 (49.4)	40 (50.6)	6.2 (4.4, 8.5)	0.6361 (0.4262, 0.9494) 0.0268	0.0244	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.1099
0	60	26 (43.3)	34 (56.7)	11.3 (6.8, NE)	34	17 (50.0)	17 (50.0)	5.4 (3.4, 7.0)	0.5067 (0.2672, 0.9612) 0.0374	0.0340
1	108	44 (40.7)	64 (59.3)	13.6 (9.0, 21.7)	51	24 (47.1)	27 (52.9)	8.5 (4.3, 18.5)	0.6647 (0.4014, 1.1005) 0.1124	0.1103
2	115	45 (39.1)	70 (60.9)	18.2 (12.5, NE)	54	30 (55.6)	24 (44.4)	4.4 (2.0, 7.9)	0.3643 (0.2221, 0.5975) 0.0001	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	41 (45.6)	49 (54.4)	12.8 (9.1, 23.0)	45	17 (37.8)	28 (62.2)	7.7 (4.2, NE)	0.8403 (0.4695, 1.5038) 0.5579	0.5420	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.8604
PD	174	65 (37.4)	109 (62.6)	13.6 (10.8, 21.5)	85	39 (45.9)	46 (54.1)	5.8 (4.6, 8.5)	0.5246 (0.3469, 0.7933) 0.0022	0.0018	
PR	48	24 (50.0)	24 (50.0)	13.2 (4.2, NE)	22	10 (45.5)	12 (54.5)	5.7 (1.0, NE)	0.6093 (0.2871, 1.2929) 0.1968	0.1939	
SD	82	29 (35.4)	53 (64.6)	21.7 (12.7, NE)	55	28 (50.9)	27 (49.1)	6.1 (4.4, 11.3)	0.4678 (0.2736, 0.7999) 0.0055	0.0046	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.0463
Yes	37	17 (45.9)	20 (54.1)	11.2 (1.6, NE)	15	3 (20.0)	12 (80.0)	NE (2.1, NE)	1.9817 (0.5785, 6.7891) 0.2763	0.2706	
No	336	139 (41.4)	197 (58.6)	13.8 (11.3, 18.2)	169	85 (50.3)	84 (49.7)	5.8 (4.4, 7.7)	0.5129 (0.3882, 0.6778) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	No. of subjects	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Baseline CNS metastases										0.0059
Yes	24	13 (54.2)	11 (45.8)	3.0 (0.9, NE)	8	1 (12.5)	7 (87.5)	NE (4.7, NE)	4.9290 (0.6415, 37.8736)	0.0893
No	349	143 (41.0)	206 (59.0)	13.8 (12.5, 19.3)	176	87 (49.4)	89 (50.6)	5.9 (4.4, 7.7)	0.5107 (0.3878, 0.6724)	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0376
Normal Function	202	83 (41.1)	119 (58.9)	15.2 (10.4, 21.7)	87	48 (55.2)	39 (44.8)	4.4 (2.9, 5.4)	0.4422 (0.3065, 0.6380) <0.0001	<0.0001	
Mild Impairment	123	54 (43.9)	69 (56.1)	13.1 (10.8, 19.3)	69	30 (43.5)	39 (56.5)	6.1 (4.2, NE)	0.5537 (0.3435, 0.8924) 0.0152	0.0133	
Moderate Impairment	41	17 (41.5)	24 (58.5)	13.6 (6.8, NE)	23	8 (34.8)	15 (65.2)	18.5 (7.0, 18.5)	1.2253 (0.5266, 2.8512) 0.6372	0.6357	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.8617
Normal Function	170	71 (41.8)	99 (58.2)	13.8 (11.3, NE)	98	46 (46.9)	52 (53.1)	6.1 (5.4, 9.7)	0.5917 (0.4041, 0.8663) 0.0070	0.0062	
Mild Impairment	195	84 (43.1)	111 (56.9)	13.1 (10.3, 18.2)	84	42 (50.0)	42 (50.0)	4.7 (2.9, 8.5)	0.5149 (0.3509, 0.7555) 0.0007	0.0005	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.3119
Yes	332	138 (41.6)	194 (58.4)	13.6 (11.2, 19.3)	157	72 (45.9)	85 (54.1)	6.2 (4.7, 8.5)	0.5915 (0.4418, 0.7919) 0.0004	0.0003	
No	41	18 (43.9)	23 (56.1)	17.5 (5.6, NE)	27	16 (59.3)	11 (40.7)	4.6 (1.5, 7.0)	0.4761 (0.2319, 0.9775) 0.0432	0.0368	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.7465
Positive	331	140 (42.3)	191 (57.7)	13.6 (11.3, 18.2)	163	76 (46.6)	87 (53.4)	6.1 (4.6, 8.5)	0.5703 (0.4281, 0.7599) 0.0001	<0.0001	
Negative	42	16 (38.1)	26 (61.9)	NE (4.7, NE)	21	12 (57.1)	9 (42.9)	4.4 (1.7, 7.0)	0.5999 (0.2784, 1.2928) 0.1921	0.1892	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.8301
Positive	333	142 (42.6)	191 (57.4)	13.6 (11.2, 18.2)	166	79 (47.6)	87 (52.4)	6.0 (4.6, 8.4)	0.5695 (0.4291, 0.7557) 0.0001	<0.0001	
Negative	40	14 (35.0)	26 (65.0)	NE (4.7, NE)	18	9 (50.0)	9 (50.0)	5.3 (1.7, NE)	0.5730 (0.2429, 1.3514) 0.2034	0.1966	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.1322
HER2 IHC 1+	214	62 (29.0)	152 (71.0)	22.3 (17.6, NE)	107	36 (33.6)	71 (66.4)	11.3 (6.8, 14.0)	0.4997 (0.3267, 0.7643) 0.0014	0.0011
HER2 IHC 2+/ISH Negative	159	57 (35.8)	102 (64.2)	20.7 (12.7, NE)	77	23 (29.9)	54 (70.1)	NE (6.7, NE)	0.8496 (0.5191, 1.3906) 0.5168	0.5132

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.1264
1	221	75 (33.9)	146 (66.1)	18.3 (16.3, NE)	100	29 (29.0)	71 (71.0)	11.4 (9.0, NE)	0.8210 (0.5310, 1.2693) 0.3749	0.3723
>=2	151	44 (29.1)	107 (70.9)	20.0 (17.6, NE)	83	30 (36.1)	53 (63.9)	7.5 (4.4, NE)	0.4374 (0.2686, 0.7122) 0.0009	0.0006

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Prior CDK4/6											
Yes	235	74 (31.5)	161 (68.5)	22.3 (13.0, NE)	118	35 (29.7)	83 (70.3)	9.3 (6.8, NE)	0.6825 (0.4526, 1.0293) 0.0684	0.0663	0.5488
No	98	32 (32.7)	66 (67.3)	20.7 (18.7, NE)	48	18 (37.5)	30 (62.5)	11.4 (6.1, NE)	0.5099 (0.2797, 0.9297) 0.0280	0.0251	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Age										0.4137
<65	290	88 (30.3)	202 (69.7)	22.3 (17.6, NE)	136	42 (30.9)	94 (69.1)	9.3 (6.8, NE)	0.5966 (0.4089, 0.8703)	0.0065
>=65	83	31 (37.3)	52 (62.7)	17.8 (10.0, NE)	48	17 (35.4)	31 (64.6)	11.4 (6.7, NE)	0.7624 (0.4150, 1.4007)	0.3791

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Age											
<75	359	113 (31.5)	246 (68.5)	22.3 (18.3, NE)	175	56 (32.0)	119 (68.0)	11.4 (7.5, NE)	0.6121 (0.4405, 0.8507) 0.0035	0.0031	0.2330
>=75	14	6 (42.9)	8 (57.1)	16.7 (4.2, 17.8)	9	3 (33.3)	6 (66.7)	11.3 (3.8, NE)	1.2006 (0.2836, 5.0829) 0.8038	0.8036	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Race										0.2249
White	176	55 (31.3)	121 (68.8)	20.0 (16.7, NE)	91	23 (25.3)	68 (74.7)	NE (7.7, NE)	0.8127 (0.4940, 1.3368) 0.4140	0.4132
Non-White	197	64 (32.5)	133 (67.5)	20.7 (17.8, NE)	92	36 (39.1)	56 (60.9)	11.3 (6.1, 14.0)	0.5195 (0.3415, 0.7903) 0.0022	0.0018

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.8576
Asia	147	53 (36.1)	94 (63.9)	20.7 (16.3, NE)	66	26 (39.4)	40 (60.6)	11.3 (5.9, NE)	0.5744 (0.3554, 0.9284) 0.0236	0.0219	
North America	60	14 (23.3)	46 (76.7)	22.3 (11.2, NE)	33	7 (21.2)	26 (78.8)	NE (3.7, NE)	0.6513 (0.2541, 1.6693) 0.3719	0.3687	
Europe + Israel	166	52 (31.3)	114 (68.7)	18.7 (16.7, NE)	85	26 (30.6)	59 (69.4)	11.4 (6.8, NE)	0.6903 (0.4262, 1.1179) 0.1319	0.1289	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	200	61 (30.5)	139 (69.5)	23.8 (17.8, NE)	105	35 (33.3)	70 (66.7)	11.4 (6.7, NE)	0.5080 (0.3320, 0.7774) 0.0018	0.0015	0.1315
1	173	58 (33.5)	115 (66.5)	18.7 (17.6, NE)	79	24 (30.4)	55 (69.6)	11.3 (6.8, NE)	0.8386 (0.5146, 1.3667) 0.4799	0.4724	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.7612
0	60	20 (33.3)	40 (66.7)	17.6 (7.8, NE)	34	10 (29.4)	24 (70.6)	NE (3.8, NE)	0.6976 (0.3185, 1.5279) 0.3680	0.3673	
1	108	37 (34.3)	71 (65.7)	18.7 (12.7, NE)	51	19 (37.3)	32 (62.7)	11.4 (6.1, NE)	0.7632 (0.4359, 1.3364) 0.3444	0.3419	
2	115	34 (29.6)	81 (70.4)	22.3 (16.7, NE)	54	18 (33.3)	36 (66.7)	7.5 (6.7, NE)	0.4843 (0.2662, 0.8812) 0.0176	0.0151	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	28 (31.1)	62 (68.9)	20.7 (16.3, NE)	45	12 (26.7)	33 (73.3)	NE (7.7, NE)	0.6889 (0.3439, 1.3801) 0.2931	0.2875

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.0812
PD	174	48 (27.6)	126 (72.4)	18.7 (16.3, NE)	85	32 (37.6)	53 (62.4)	7.5 (4.4, NE)	0.4305 (0.2700, 0.6866) 0.0004	0.0003	
PR	48	18 (37.5)	30 (62.5)	20.7 (11.2, NE)	22	7 (31.8)	15 (68.2)	11.7 (3.8, NE)	0.5524 (0.2220, 1.3745) 0.2019	0.1945	
SD	82	30 (36.6)	52 (63.4)	20.0 (14.1, NE)	55	14 (25.5)	41 (74.5)	14.0 (9.0, NE)	1.0343 (0.5406, 1.9790) 0.9188	0.9232	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.4651
Yes	37	9 (24.3)	28 (75.7)	NE (11.2, NE)	15	4 (26.7)	11 (73.3)	NE (1.0, NE)	0.5203 (0.1558, 1.7376) 0.2883	0.2795	
No	336	110 (32.7)	226 (67.3)	20.0 (17.6, NE)	169	55 (32.5)	114 (67.5)	11.4 (7.7, NE)	0.6460 (0.4634, 0.9006) 0.0099	0.0092	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.2872
Yes	24	8 (33.3)	16 (66.7)	NE (5.4, NE)	8	1 (12.5)	7 (87.5)	NE (1.4, NE)	1.6089 (0.1966, 13.1657) 0.6575	0.6545
No	349	111 (31.8)	238 (68.2)	20.0 (17.6, NE)	176	58 (33.0)	118 (67.0)	11.3 (7.5, NE)	0.6138 (0.4430, 0.8503) 0.0033	0.0030

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0325
Normal Function	202	57 (28.2)	145 (71.8)	NE (18.3, NE)	87	31 (35.6)	56 (64.4)	7.7 (4.9, NE)	0.4797 (0.3058, 0.7524) 0.0014	0.0011	
Mild Impairment	123	44 (35.8)	79 (64.2)	17.8 (12.5, NE)	69	20 (29.0)	49 (71.0)	11.7 (6.8, NE)	0.7507 (0.4329, 1.3017) 0.3072	0.3020	
Moderate Impairment	41	16 (39.0)	25 (61.0)	16.7 (11.2, NE)	23	5 (21.7)	18 (78.3)	NE (11.3, NE)	1.5831 (0.5746, 4.3612) 0.3743	0.3698	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.5046
Normal Function	170	54 (31.8)	116 (68.2)	22.3 (18.3, NE)	98	34 (34.7)	64 (65.3)	11.4 (7.0, NE)	0.5926 (0.3818, 0.9196) 0.0196	0.0180
Mild Impairment	195	63 (32.3)	132 (67.7)	17.6 (13.0, NE)	84	24 (28.6)	60 (71.4)	11.3 (5.3, NE)	0.6813 (0.4204, 1.1042) 0.1194	0.1165

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline visceral disease										0.1145
Yes	332	109 (32.8)	223 (67.2)	20.0 (17.6, NE)	157	48 (30.6)	109 (69.4)	11.4 (7.7, NE)	0.6983 (0.4937, 0.9876)	0.0411 (0.0423)
No	41	10 (24.4)	31 (75.6)	NE (13.0, NE)	27	11 (40.7)	16 (59.3)	6.7 (4.4, 14.0)	0.3048 (0.1200, 0.7739)	0.0085 (0.0124)

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (IXRS)										0.6995
Positive	331	104 (31.4)	227 (68.6)	20.7 (18.3, NE)	163	52 (31.9)	111 (68.1)	11.4 (7.7, NE)	0.6197 (0.4408, 0.8711) 0.0059	0.0054
Negative	42	15 (35.7)	27 (64.3)	17.6 (5.6, NE)	21	7 (33.3)	14 (66.7)	NE (3.4, NE)	0.7775 (0.3053, 1.9802) 0.5978	0.5944

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.7672
Positive	333	105 (31.5)	228 (68.5)	20.7 (18.3, NE)	166	53 (31.9)	113 (68.1)	11.4 (7.7, NE)	0.6222 (0.4437, 0.8725) 0.0060	0.0055	
Negative	40	14 (35.0)	26 (65.0)	17.6 (6.4, NE)	18	6 (33.3)	12 (66.7)	NE (1.7, NE)	0.7442 (0.2756, 2.0094) 0.5599	0.5558	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.1459
HER2 IHC 1+	214	111 (51.9)	103 (48.1)	7.5 (3.2, 10.4)	107	29 (27.1)	78 (72.9)	11.3 (8.6, NE)	1.8893 (1.2519, 2.8511) 0.0024	0.0022
HER2 IHC 2+/ISH Negative	159	76 (47.8)	83 (52.2)	7.5 (4.2, NE)	77	29 (37.7)	48 (62.3)	9.0 (5.9, 21.9)	1.2351 (0.8046, 1.8958) 0.3342	0.3381

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.7042
1	221	105 (47.5)	116 (52.5)	8.4 (3.4, NE)	100	33 (33.0)	67 (67.0)	11.3 (8.2, 21.9)	1.4712 (0.9935, 2.1786) 0.0540	0.0555
>=2	151	81 (53.6)	70 (46.4)	6.2 (4.2, 11.1)	83	25 (30.1)	58 (69.9)	17.1 (7.5, NE)	1.6350 (1.0405, 2.5692) 0.0330	0.0326

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.1907
Yes	235	116 (49.4)	119 (50.6)	7.6 (4.4, 19.6)	118	39 (33.1)	79 (66.9)	9.5 (5.9, 21.9)	1.3367 (0.9277, 1.9261) 0.1194	0.1220	
No	98	54 (55.1)	44 (44.9)	5.7 (1.5, NE)	48	14 (29.2)	34 (70.8)	NE (8.2, NE)	2.1282 (1.1810, 3.8351) 0.0119	0.0106	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3711
<65	290	150 (51.7)	140 (48.3)	6.2 (4.3, 10.4)	136	40 (29.4)	96 (70.6)	13.3 (8.6, 21.9)	1.6754 (1.1800, 2.3788) 0.0039	0.0038	
>=65	83	37 (44.6)	46 (55.4)	9.3 (2.8, NE)	48	18 (37.5)	30 (62.5)	9.5 (5.9, NE)	1.2496 (0.7094, 2.2012) 0.4406	0.4479	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Age										0.2048
<75	359	178 (49.6)	181 (50.4)	7.6 (5.3, 14.3)	175	55 (31.4)	120 (68.6)	9.5 (8.6, 21.9)	1.4920 (1.1008, 2.0222) 0.0099	0.0101
>=75	14	9 (64.3)	5 (35.7)	2.8 (1.4, NE)	9	3 (33.3)	6 (66.7)	11.3 (6.7, NE)	4.3497 (1.1467, 16.4998) 0.0307	0.0198

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.9820
White	176	92 (52.3)	84 (47.7)	5.3 (3.0, 8.4)	91	29 (31.9)	62 (68.1)	9.0 (5.6, NE)	1.5595 (1.0249, 2.3730) 0.0380	0.0382	
Non-White	197	95 (48.2)	102 (51.8)	9.9 (5.7, NE)	92	29 (31.5)	63 (68.5)	11.3 (8.6, 21.9)	1.5235 (1.0033, 2.3135) 0.0482	0.0486	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Region										0.6814
Asia	147	72 (49.0)	75 (51.0)	10.2 (5.7, NE)	66	23 (34.8)	43 (65.2)	11.3 (8.6, 21.9)	1.3510 (0.8429, 2.1654) 0.2113	0.2158
North America	60	31 (51.7)	29 (48.3)	4.2 (1.6, 22.3)	33	7 (21.2)	26 (78.8)	13.3 (5.9, 13.3)	2.1219 (0.9286, 4.8487) 0.0744	0.0686
Europe + Israel	166	84 (50.6)	82 (49.4)	6.2 (3.0, 17.6)	85	28 (32.9)	57 (67.1)	9.0 (5.9, NE)	1.5860 (1.0318, 2.4381) 0.0355	0.0355

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.6292
0	200	100 (50.0)	100 (50.0)	8.4 (3.1, 23.0)	105	33 (31.4)	72 (68.6)	9.3 (6.7, 21.9)	1.4764 (0.9941, 2.1927) 0.0536	0.0543	
1	173	87 (50.3)	86 (49.7)	6.2 (4.2, 10.2)	79	25 (31.6)	54 (68.4)	11.3 (8.6, 17.1)	1.6486 (1.0537, 2.5793) 0.0286	0.0283	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.4213
0	60	29 (48.3)	31 (51.7)	11.1 (1.4, NE)	34	9 (26.5)	25 (73.5)	9.0 (5.9, NE)	1.6774 (0.7920, 3.5527) 0.1767	0.1730	
1	108	54 (50.0)	54 (50.0)	6.7 (2.8, 10.4)	51	14 (27.5)	37 (72.5)	17.1 (9.0, NE)	2.2787 (1.2646, 4.1060) 0.0061	0.0050	
2	115	56 (48.7)	59 (51.3)	7.8 (4.2, NE)	54	17 (31.5)	37 (68.5)	NE (5.1, NE)	1.3906 (0.8053, 2.4015) 0.2368	0.2394	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	48 (53.3)	42 (46.7)	7.6 (3.4, 23.0)	45	18 (40.0)	27 (60.0)	8.6 (5.6, 21.9)	1.1898 (0.6885, 2.0562) 0.5334	0.5473

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy									0.5954
PD	174	77 (44.3)	97 (55.7) (4.3, NE)	85	27 (31.8)	58 (68.2) (5.4, NE)	1.2630 (0.8133, 1.9612) 0.2985	0.3017	
PR	48	29 (60.4)	19 (39.6) (1.4, 22.3)	22	8 (36.4)	14 (63.6) (4.2, NE)	1.5437 (0.7024, 3.3930) 0.2799	0.2837	
SD	82	38 (46.3)	44 (53.7) (3.2, NE)	55	15 (27.3)	40 (72.7) (9.0, 21.9)	1.7640 (0.9673, 3.2170) 0.0641	0.0617	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.5995
Yes	37	20 (54.1)	17 (45.9)	5.7 (1.4, NE)	15	3 (20.0)	12 (80.0)	17.1 (1.4, 17.1)	2.2855 (0.6752, 7.7359) 0.1839	0.1744
No	336	167 (49.7)	169 (50.3)	7.5 (4.3, 11.1)	169	55 (32.5)	114 (67.5)	9.5 (8.6, 21.9)	1.5128 (1.1136, 2.0550) 0.0081	0.0082

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.5492
Yes	24	9 (37.5)	15 (62.5)	NE (2.8, NE)	8	1 (12.5)	7 (87.5)	17.1 (NE, NE)	3.2147 (0.4063, 25.4323)	0.2423
No	349	178 (51.0)	171 (49.0)	6.7 (4.2, 10.2)	176	57 (32.4)	119 (67.6)	9.5 (8.2, 21.9)	1.5413 (1.1421, 2.0800)	0.0047

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Renal function at baseline										0.9905
Normal Function	202	104 (51.5)	98 (48.5)	5.8 (4.2, 19.6)	87	27 (31.0)	60 (69.0)	13.3 (6.7, 21.9)	1.5619 (1.0214, 2.3882) 0.0396	0.0395
Mild Impairment	123	64 (52.0)	59 (48.0)	7.6 (2.8, 14.3)	69	22 (31.9)	47 (68.1)	9.0 (6.0, NE)	1.5067 (0.9222, 2.4616) 0.1017	0.1027
Moderate Impairment	41	18 (43.9)	23 (56.1)	NE (3.0, NE)	23	8 (34.8)	15 (65.2)	17.1 (8.2, NE)	1.6762 (0.7259, 3.8705) 0.2264	0.2256

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.8322
Normal Function	170	94 (55.3)	76 (44.7)	5.5 (1.7, 11.1)	98	35 (35.7)	63 (64.3)	9.0 (8.0, 21.9)	1.6114 (1.0907, 2.3808) 0.0166	0.0171
Mild Impairment	195	91 (46.7)	104 (53.3)	7.8 (5.7, 19.6)	84	23 (27.4)	61 (72.6)	11.3 (9.3, NE)	1.4787 (0.9333, 2.3429) 0.0957	0.0951

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.3014
Yes	332	165 (49.7)	167 (50.3)	7.6 (5.3, 11.1)	157	45 (28.7)	112 (71.3)	13.3 (8.6, 21.9)	1.6845 (1.2096, 2.3458) 0.0020	0.0019	
No	41	22 (53.7)	19 (46.3)	4.2 (1.0, NE)	27	13 (48.1)	14 (51.9)	6.7 (1.5, NE)	1.1627 (0.5814, 2.3250) 0.6699	0.6809	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (IXRS)										0.8934
Positive	331	169 (51.1)	162 (48.9)	6.7 (4.3, 10.2)	163	52 (31.9)	111 (68.1)	11.3 (8.6, 21.9)	1.5629 (1.1438, 2.1356) 0.0051	0.0050
Negative	42	18 (42.9)	24 (57.1)	14.3 (1.4, NE)	21	6 (28.6)	15 (71.4)	9.0 (5.9, NE)	1.4502 (0.5664, 3.7127) 0.4384	0.4433

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (derived)										0.7776
Positive	333	168 (50.5)	165 (49.5)	7.5 (4.3, 10.4)	166	53 (31.9)	113 (68.1)	11.3 (8.6, 21.9)	1.5327 (1.1239, 2.0903) 0.0070	0.0070
Negative	40	19 (47.5)	21 (52.5)	14.3 (1.4, NE)	18	5 (27.8)	13 (72.2)	9.0 (5.9, NE)	1.6990 (0.6262, 4.6094) 0.2980	0.2984

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status									0.2886
HER2 IHC 1+	214	81 (37.9)	133 (62.1)	107	44 (41.1)	63 (58.9)	7.3 (4.4, 9.3)	0.4738 (0.3209, 0.6995)	0.0002
HER2 IHC 2+/ISH Negative	159	47 (29.6)	112 (70.4)	77	36 (46.8)	41 (53.2)	6.1 (4.2, 14.7)	0.3628 (0.2313, 0.5689)	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.9266
1	221	81 (36.7)	140 (63.3)	16.4 (13.3, 20.0)	100	48 (48.0)	52 (52.0)	5.8 (3.0, 8.7)	0.4034 (0.2774, 0.5866) <0.0001	<0.0001	
>=2	151	46 (30.5)	105 (69.5)	23.0 (17.6, 27.2)	83	32 (38.6)	51 (61.4)	7.5 (4.4, 9.8)	0.4442 (0.2768, 0.7130) 0.0008	0.0006	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.2884
Yes	235	77 (32.8)	158 (67.2)	17.0 (13.9, 23.0)	118	48 (40.7)	70 (59.3)	7.3 (4.5, 9.3)	0.4315 (0.2958, 0.6294) <0.0001	<0.0001	
No	98	37 (37.8)	61 (62.2)	21.7 (13.1, 27.2)	48	26 (54.2)	22 (45.8)	5.4 (1.5, 9.8)	0.3591 (0.2132, 0.6047) 0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2737
<65	290	97 (33.4)	193 (66.6)	18.2 (15.7, 23.0)	136	61 (44.9)	75 (55.1)	5.9 (4.2, 8.7)	0.3924 (0.2808, 0.5486) <0.0001	<0.0001	
>=65	83	31 (37.3)	52 (62.7)	17.0 (10.2, NE)	48	19 (39.6)	29 (60.4)	7.5 (6.2, NE)	0.5825 (0.3207, 1.0581) 0.0760	0.0751	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3900
<75	359	125 (34.8)	234 (65.2)	17.6 (15.4, 23.0)	175	78 (44.6)	97 (55.4)	7.0 (4.5, 8.4)	0.4078 (0.3030, 0.5487) <0.0001	<0.0001	
>=75	14	3 (21.4)	11 (78.6)	NE (1.6, NE)	9	2 (22.2)	7 (77.8)	NE (0.7, NE)	1.1047 (0.1841, 6.6270) 0.9133	0.9133	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.3572
White	176	47 (26.7)	129 (73.3)	21.5 (16.4, NE)	91	34 (37.4)	57 (62.6)	7.7 (4.2, NE)	0.3728 (0.2350, 0.5913) <0.0001	<0.0001	
Non-White	197	81 (41.1)	116 (58.9)	17.0 (11.9, 21.7)	92	45 (48.9)	47 (51.1)	6.2 (4.4, 9.3)	0.4928 (0.3371, 0.7202) 0.0003	0.0002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.4006
Asia	147	67 (45.6)	80 (54.4)	15.7 (10.5, 21.7)	66	34 (51.5)	32 (48.5)	6.1 (2.4, 9.8)	0.4998 (0.3252, 0.7683) 0.0016	0.0013	
North America	60	11 (18.3)	49 (81.7)	21.5 (21.5, NE)	33	11 (33.3)	22 (66.7)	5.8 (2.7, NE)	0.2198 (0.0843, 0.5727) 0.0019	0.0007	
Europe + Israel	166	50 (30.1)	116 (69.9)	17.6 (15.4, NE)	85	35 (41.2)	50 (58.8)	7.5 (4.2, 16.9)	0.4325 (0.2769, 0.6754) 0.0002	0.0002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.1138
0	200	72 (36.0)	128 (64.0)	17.0 (13.9, 25.1)	105	49 (46.7)	56 (53.3)	5.8 (2.8, 8.7)	0.3390 (0.2315, 0.4965) <0.0001	<0.0001	
1	173	56 (32.4)	117 (67.6)	21.5 (13.3, NE)	79	31 (39.2)	48 (60.8)	7.5 (5.8, NE)	0.5998 (0.3811, 0.9439) 0.0272	0.0247	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.3243
0	60	24 (40.0)	36 (60.0)	17.6 (6.9, NE)	34	15 (44.1)	19 (55.9)	5.9 (1.4, NE)	0.5254 (0.2696, 1.0237) 0.0586	0.0543	
1	108	34 (31.5)	74 (68.5)	18.2 (13.1, 27.2)	51	18 (35.3)	33 (64.7)	9.3 (7.3, NE)	0.6230 (0.3472, 1.1179) 0.1127	0.1098	
2	115	38 (33.0)	77 (67.0)	21.5 (13.3, NE)	54	21 (38.9)	33 (61.1)	7.0 (2.9, NE)	0.3844 (0.2143, 0.6894) 0.0013	0.0009	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	32 (35.6)	58 (64.4)	16.7 (13.4, 25.1)	45	26 (57.8)	19 (42.2)	4.2 (2.0, 7.7)	0.2704 (0.1545, 0.4731) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.9069
PD	174	54 (31.0)	120 (69.0)	20.0 (17.0, 27.2)	85	35 (41.2)	50 (58.8)	7.3 (4.7, 8.7)	0.4223 (0.2704, 0.6595) 0.0002	<0.0001	
PR	48	16 (33.3)	32 (66.7)	16.4 (15.7, NE)	22	7 (31.8)	15 (68.2)	NE (2.8, NE)	0.5093 (0.1981, 1.3092) 0.1613	0.1459	
SD	82	30 (36.6)	52 (63.4)	21.7 (12.5, NE)	55	25 (45.5)	30 (54.5)	8.4 (4.4, 14.7)	0.4366 (0.2485, 0.7671) 0.0040	0.0031	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.0727
Yes	37	12 (32.4)	25 (67.6)	NE (8.0, NE)	15	2 (13.3)	13 (86.7)	NE (1.5, NE)	1.5158 (0.3343, 6.8725) 0.5897	0.5843	
No	336	116 (34.5)	220 (65.5)	18.2 (15.4, 23.0)	169	78 (46.2)	91 (53.8)	7.0 (4.4, 8.4)	0.3984 (0.2945, 0.5391) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0084
Yes	24	7 (29.2)	17 (70.8)	NE (5.9, NE)	8	0	8 (100)	NE (NE, NE)	NE (NE, NE) 0.9951	0.1773	
No	349	121 (34.7)	228 (65.3)	17.6 (15.4, 23.0)	176	80 (45.5)	96 (54.5)	6.2 (4.4, 8.4)	0.4025 (0.2990, 0.5417) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.1506
Normal Function	202	63 (31.2)	139 (68.8)	18.2 (15.4, NE)	87	39 (44.8)	48 (55.2)	7.2 (4.2, 9.3)	0.3229 (0.2107, 0.4947) <0.0001	<0.0001	
Mild Impairment	123	50 (40.7)	73 (59.3)	17.6 (10.0, 25.1)	69	31 (44.9)	38 (55.1)	6.1 (3.2, 16.9)	0.4926 (0.3071, 0.7902) 0.0033	0.0027	
Moderate Impairment	41	13 (31.7)	28 (68.3)	NE (11.2, NE)	23	7 (30.4)	16 (69.6)	NE (5.9, NE)	0.8920 (0.3542, 2.2466) 0.8085	0.8154	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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## Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.4033
Normal Function	170	68 (40.0)	102 (60.0)	16.7 (12.5, 25.1)	98	44 (44.9)	54 (55.1)	6.2 (4.5, 14.7)	0.5148 (0.3481, 0.7614) 0.0009	0.0007	
Mild Impairment	195	58 (29.7)	137 (70.3)	20.0 (13.9, NE)	84	34 (40.5)	50 (59.5)	7.7 (3.4, 9.3)	0.3708 (0.2358, 0.5830) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.4624
Yes	332	115 (34.6)	217 (65.4)	17.6 (13.9, 21.7)	157	68 (43.3)	89 (56.7)	7.2 (5.4, 8.7)	0.4460 (0.3265, 0.6092) <0.0001	<0.0001	
No	41	13 (31.7)	28 (68.3)	25.1 (16.7, 25.1)	27	12 (44.4)	15 (55.6)	5.9 (1.5, 9.8)	0.3303 (0.1388, 0.7859) 0.0123	0.0086	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.5594
Positive	331	114 (34.4)	217 (65.6)	18.2 (15.4, 23.0)	163	72 (44.2)	91 (55.8)	7.2 (4.5, 8.7)	0.4112 (0.3022, 0.5595) <0.0001	<0.0001	
Negative	42	14 (33.3)	28 (66.7)	25.1 (5.9, 25.1)	21	8 (38.1)	13 (61.9)	NE (1.5, NE)	0.6994 (0.2850, 1.7164) 0.4350	0.4277	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.2337
Positive	333	113 (33.9)	220 (66.1)	18.2 (15.4, 23.0)	166	74 (44.6)	92 (55.4)	7.0 (4.5, 8.4)	0.3989 (0.2936, 0.5419) <0.0001	<0.0001	
Negative	40	15 (37.5)	25 (62.5)	17.6 (5.4, 25.1)	18	6 (33.3)	12 (66.7)	NE (1.5, NE)	0.9403 (0.3565, 2.4800) 0.9010	0.8945	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.3909
HER2 IHC 1+	214	70 (32.7)	144 (67.3)	24.1 (13.2, NE)	107	23 (21.5)	84 (78.5)	NE (NE, NE)	1.0077 (0.6247, 1.6258) 0.9748	0.9757
HER2 IHC 2+/ISH Negative	159	52 (32.7)	107 (67.3)	21.7 (12.6, NE)	77	24 (31.2)	53 (68.8)	9.4 (6.5, NE)	0.7134 (0.4357, 1.1680) 0.1794	0.1739

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.2868
1	221	77 (34.8)	144 (65.2)	21.7 (13.2, NE)	100	25 (25.0)	75 (75.0)	NE (NE, NE)	1.0494 (0.6649, 1.6563) 0.8358	0.8402
>=2	151	45 (29.8)	106 (70.2)	27.2 (12.6, NE)	83	22 (26.5)	61 (73.5)	13.7 (6.2, NE)	0.6331 (0.3754, 1.0676) 0.0864	0.0840

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.6026
Yes	235	74 (31.5)	161 (68.5)	21.7 (13.2, NE)	118	30 (25.4)	88 (74.6)	NE (6.5, NE)	0.7888 (0.5118, 1.2157) 0.2824	0.2805	
No	98	37 (37.8)	61 (62.2)	27.2 (12.0, 27.2)	48	13 (27.1)	35 (72.9)	NE (8.3, NE)	0.9840 (0.5197, 1.8632) 0.9605	0.9610	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7482
<65	290	96 (33.1)	194 (66.9)	18.0 (14.1, 27.2)	136	32 (23.5)	104 (76.5)	NE (NE, NE)	0.8659 (0.5759, 1.3020) 0.4891	0.4853	
>=65	83	26 (31.3)	57 (68.7)	NE (11.1, NE)	48	15 (31.3)	33 (68.8)	13.7 (7.5, NE)	0.8514 (0.4486, 1.6159) 0.6227	0.6220	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4669
<75	359	116 (32.3)	243 (67.7)	21.7 (15.9, NE)	175	43 (24.6)	132 (75.4)	NE (NE, NE)	0.8441 (0.5911, 1.2053) 0.3510	0.3480	
>=75	14	6 (42.9)	8 (57.1)	11.1 (0.9, NE)	9	4 (44.4)	5 (55.6)	13.7 (3.8, NE)	1.2901 (0.3624, 4.5921) 0.6942	0.6934	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Race										0.2573
White	176	49 (27.8)	127 (72.2)	NE (16.7, NE)	91	23 (25.3)	68 (74.7)	NE (6.2, NE)	0.6875 (0.4140, 1.1417) 0.1476	0.1444
Non-White	197	73 (37.1)	124 (62.9)	18.0 (11.8, 27.2)	92	24 (26.1)	68 (73.9)	NE (13.7, NE)	1.0167 (0.6374, 1.6217) 0.9446	0.9460

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.0777
Asia	147	61 (41.5)	86 (58.5)	15.9 (11.1, 27.2)	66	16 (24.2)	50 (75.8)	NE (13.7, NE)	1.2888 (0.7389, 2.2480) 0.3713	0.3706	
North America	60	13 (21.7)	47 (78.3)	NE (12.5, NE)	33	9 (27.3)	24 (72.7)	NE (3.7, NE)	0.4074 (0.1680, 0.9881) 0.0470	0.0412	
Europe + Israel	166	48 (28.9)	118 (71.1)	21.7 (16.7, NE)	85	22 (25.9)	63 (74.1)	NE (6.5, NE)	0.7304 (0.4361, 1.2234) 0.2326	0.2290	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
ECOG PS										0.3294
0	200	73 (36.5)	127 (63.5)	18.0 (13.2, 27.2)	105	23 (21.9)	82 (78.1)	NE (13.7, NE)	0.9812 (0.6085, 1.5822)	0.9359
1	173	49 (28.3)	124 (71.7)	NE (NE, NE)	79	24 (30.4)	55 (69.6)	NE (6.2, NE)	0.7536 (0.4602, 1.2340)	0.2555

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.6712
0	60	18 (30.0)	42 (70.0)	NE (11.1, NE)	34	8 (23.5)	26 (76.5)	NE (5.9, NE)	0.7320 (0.3087, 1.7359) 0.4789	0.4777	
1	108	34 (31.5)	74 (68.5)	21.7 (12.0, 27.2)	51	11 (21.6)	40 (78.4)	NE (NE, NE)	1.1267 (0.5646, 2.2484) 0.7351	0.7359	
2	115	42 (36.5)	73 (63.5)	16.7 (11.1, NE)	54	17 (31.5)	37 (68.5)	7.5 (5.0, NE)	0.6429 (0.3587, 1.1522) 0.1378	0.1328	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	28 (31.1)	62 (68.9)	NE (15.9, NE)	45	11 (24.4)	34 (75.6)	13.7 (6.2, NE)	0.8421 (0.4149, 1.7093) 0.6342	0.6328

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.9631
PD	174	51 (29.3)	123 (70.7)	24.1 (18.0, NE)	85	21 (24.7)	64 (75.3)	NE (7.5, NE)	0.7827 (0.4661, 1.3143) 0.3541	0.3512
PR	48	16 (33.3)	32 (66.7)	NE (10.4, NE)	22	6 (27.3)	16 (72.7)	NE (3.8, NE)	0.7773 (0.2964, 2.0388) 0.6086	0.6054
SD	82	25 (30.5)	57 (69.5)	NE (12.5, NE)	55	14 (25.5)	41 (74.5)	NE (8.3, NE)	0.8398 (0.4315, 1.6345) 0.6073	0.6043

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.7919
Yes	37	7 (18.9)	30 (81.1)	NE (NE, NE)	15	2 (13.3)	13 (86.7)	NE (1.5, NE)	0.8536 (0.1732, 4.2066)	0.8486
No	336	115 (34.2)	221 (65.8)	21.7 (13.2, NE)	169	45 (26.6)	124 (73.4)	NE (9.4, NE)	0.8745 (0.6159, 1.2417)	0.4497

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.6979
Yes	24	6 (25.0)	18 (75.0)	NE (9.6, NE)	8	1 (12.5)	7 (87.5)	NE (0.7, NE)	1.3317 (0.1575, 11.2572) 0.7925	0.7841
No	349	116 (33.2)	233 (66.8)	21.7 (14.1, NE)	176	46 (26.1)	130 (73.9)	NE (9.4, NE)	0.8478 (0.5989, 1.1999) 0.3515	0.3478

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.4641
Normal Function	202	57 (28.2)	145 (71.8)	NE (16.7, NE)	87	21 (24.1)	66 (75.9)	NE (6.7, NE)	0.7327 (0.4410, 1.2172) 0.2298	0.2255	
Mild Impairment	123	47 (38.2)	76 (61.8)	15.9 (11.8, NE)	69	16 (23.2)	53 (76.8)	NE (6.5, NE)	0.9770 (0.5421, 1.7607) 0.9382	0.9350	
Moderate Impairment	41	15 (36.6)	26 (63.4)	NE (8.5, NE)	23	7 (30.4)	16 (69.6)	NE (9.4, NE)	1.3116 (0.5342, 3.2201) 0.5539	0.5523	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.5559
Normal Function	170	65 (38.2)	105 (61.8)	18.0 (12.0, NE)	98	27 (27.6)	71 (72.4)	NE (9.4, NE)	0.9545 (0.6061, 1.5032) 0.8407	0.8399	
Mild Impairment	195	55 (28.2)	140 (71.8)	21.7 (16.7, NE)	84	19 (22.6)	65 (77.4)	NE (6.5, NE)	0.7939 (0.4659, 1.3528) 0.3960	0.3919	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.8010
Yes	332	107 (32.2)	225 (67.8)	21.7 (15.9, 27.2)	157	40 (25.5)	117 (74.5)	NE (13.7, NE)	0.8227 (0.5688, 1.1898) 0.2998	0.2965	
No	41	15 (36.6)	26 (63.4)	NE (5.8, NE)	27	7 (25.9)	20 (74.1)	9.4 (5.9, NE)	1.1790 (0.4733, 2.9366) 0.7236	0.7271	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (IXRS)										0.7429
Positive	331	109 (32.9)	222 (67.1)	21.7 (15.9, NE)	163	42 (25.8)	121 (74.2)	NE (13.7, NE)	0.8394 (0.5848, 1.2048) 0.3424	0.3402
Negative	42	13 (31.0)	29 (69.0)	NE (7.8, NE)	21	5 (23.8)	16 (76.2)	9.4 (5.9, NE)	1.0298 (0.3533, 3.0013) 0.9571	0.9644

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (derived)										0.9455
Positive	333	111 (33.3)	222 (66.7)	21.7 (15.9, NE)	166	43 (25.9)	123 (74.1)	NE (13.7, NE)	0.8546 (0.5977, 1.2218)	0.3862
Negative	40	11 (27.5)	29 (72.5)	NE (11.1, NE)	18	4 (22.2)	14 (77.8)	9.4 (5.9, NE)	0.8622 (0.2614, 2.8441)	0.7976

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.0467
HER2 IHC 1+	214	70 (32.7)	144 (67.3)	18.6 (16.3, NE)	107	31 (29.0)	76 (71.0)	10.2 (5.8, NE)	0.7427 (0.4814, 1.1459)	0.1757
HER2 IHC 2+/ISH Negative	159	38 (23.9)	121 (76.1)	NE (18.3, NE)	77	29 (37.7)	48 (62.3)	8.3 (5.3, NE)	0.3717 (0.2265, 0.6102)	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.1610
1	221	64 (29.0)	157 (71.0)	NE (18.3, NE)	100	30 (30.0)	70 (70.0)	10.2 (8.3, NE)	0.7155 (0.4615, 1.1092)	0.1319
>=2	151	44 (29.1)	107 (70.9)	18.6 (16.1, NE)	83	30 (36.1)	53 (63.9)	6.9 (5.3, NE)	0.3872 (0.2365, 0.6340)	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Prior CDK4/6										0.6392
Yes	235	61 (26.0)	174 (74.0)	NE (21.7, NE)	118	33 (28.0)	85 (72.0)	10.2 (7.1, NE)	0.6287 (0.4079, 0.9688)	0.0335
No	98	35 (35.7)	63 (64.3)	18.6 (16.0, NE)	48	21 (43.8)	27 (56.3)	6.1 (4.7, NE)	0.4856 (0.2797, 0.8431)	0.0090

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1873
<65	290	82 (28.3)	208 (71.7)	NE (18.3, NE)	136	46 (33.8)	90 (66.2)	10.0 (5.7, NE)	0.4993 (0.3445, 0.7236) 0.0002	0.0002	
>=65	83	26 (31.3)	57 (68.7)	18.6 (11.1, NE)	48	14 (29.2)	34 (70.8)	11.7 (8.3, NE)	0.7661 (0.3935, 1.4913) 0.4330	0.4288	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1622
<75	359	102 (28.4)	257 (71.6)	NE (18.3, NE)	175	57 (32.6)	118 (67.4)	10.0 (6.1, NE)	0.5195 (0.3719, 0.7256) 0.0001	<0.0001	
>=75	14	6 (42.9)	8 (57.1)	5.8 (4.2, NE)	9	3 (33.3)	6 (66.7)	NE (0.8, NE)	1.3820 (0.3451, 5.5353) 0.6477	0.6557	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.1568
White	176	51 (29.0)	125 (71.0)	21.7 (16.0, NE)	91	34 (37.4)	57 (62.6)	5.9 (4.7, NE)	0.4248 (0.2691, 0.6704) 0.0002	0.0002	
Non-White	197	57 (28.9)	140 (71.1)	NE (16.6, NE)	92	26 (28.3)	66 (71.7)	11.7 (8.3, NE)	0.7055 (0.4405, 1.1299) 0.1466	0.1453	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Region										0.8070
Asia	147	45 (30.6)	102 (69.4)	NE (16.3, NE)	66	22 (33.3)	44 (66.7)	NE (6.1, NE)	0.6432 (0.3837, 1.0783) 0.0941	0.0918
North America	60	12 (20.0)	48 (80.0)	NE (NE, NE)	33	8 (24.2)	25 (75.8)	NE (3.1, NE)	0.5716 (0.2311, 1.4137) 0.2261	0.2184
Europe + Israel	166	51 (30.7)	115 (69.3)	18.3 (16.0, NE)	85	30 (35.3)	55 (64.7)	10.0 (5.4, 11.7)	0.4707 (0.2929, 0.7565) 0.0019	0.0015

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.4129
0	200	56 (28.0)	144 (72.0)	NE (18.6, NE)	105	34 (32.4)	71 (67.6)	10.0 (5.8, NE)	0.4802 (0.3103, 0.7430) 0.0010	0.0008	
1	173	52 (30.1)	121 (69.9)	NE (16.6, NE)	79	26 (32.9)	53 (67.1)	10.2 (6.1, NE)	0.6624 (0.4085, 1.0743) 0.0950	0.0926	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.6248
0	60	20 (33.3)	40 (66.7)	17.6 (9.7, NE)	34	13 (38.2)	21 (61.8)	5.4 (3.0, NE)	0.4081 (0.1973, 0.8443)	0.0129
1	108	28 (25.9)	80 (74.1)	21.7 (16.6, NE)	51	14 (27.5)	37 (72.5)	10.2 (7.1, NE)	0.7466 (0.3885, 1.4348)	0.3766
2	115	33 (28.7)	82 (71.3)	NE (NE, NE)	54	19 (35.2)	35 (64.8)	11.7 (4.5, 11.7)	0.5280 (0.2961, 0.9417)	0.0274

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	27 (30.0)	63 (70.0)	18.6 (16.1, NE)	45	14 (31.1)	31 (68.9)	9.1 (5.8, NE)	0.5070 (0.2594, 0.9910)	0.0470	0.0439

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.3244
PD	174	45 (25.9)	129 (74.1)	NE (16.3, NE)	85	25 (29.4)	60 (70.6)	NE (5.4, NE)	0.5015 (0.3024, 0.8316) 0.0075	0.0065
PR	48	12 (25.0)	36 (75.0)	NE (16.0, NE)	22	9 (40.9)	13 (59.1)	5.8 (2.8, NE)	0.2781 (0.1101, 0.7026) 0.0068	0.0038
SD	82	25 (30.5)	57 (69.5)	NE (17.6, NE)	55	17 (30.9)	38 (69.1)	10.2 (8.3, NE)	0.6886 (0.3663, 1.2945) 0.2467	0.2429

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.3094
Yes	37	11 (29.7)	26 (70.3)	NE (7.3, NE)	15	2 (13.3)	13 (86.7)	NE (2.8, NE)	1.1567 (0.2516, 5.3188) 0.8516	0.8515	
No	336	97 (28.9)	239 (71.1)	21.7 (17.6, NE)	169	58 (34.3)	111 (65.7)	10.0 (6.1, NE)	0.5316 (0.3805, 0.7426) 0.0002	0.0002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.3658
Yes	24	6 (25.0)	18 (75.0)	NE (9.6, NE)	8	1 (12.5)	7 (87.5)	NE (2.8, NE)	1.0983 (0.1274, 9.4689) 0.9320	0.9320	
No	349	102 (29.2)	247 (70.8)	NE (17.6, NE)	176	59 (33.5)	117 (66.5)	10.0 (6.1, NE)	0.5457 (0.3927, 0.7584) 0.0003	0.0003	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Renal function at baseline										0.3866
Normal Function	202	58 (28.7)	144 (71.3)	NE (18.3, NE)	87	27 (31.0)	60 (69.0)	NE (5.4, NE)	0.5563 (0.3486, 0.8877) 0.0139	0.0124
Mild Impairment	123	36 (29.3)	87 (70.7)	NE (16.3, NE)	69	24 (34.8)	45 (65.2)	9.1 (5.8, 11.7)	0.4627 (0.2681, 0.7984) 0.0056	0.0047
Moderate Impairment	41	12 (29.3)	29 (70.7)	NE (9.3, NE)	23	6 (26.1)	17 (73.9)	NE (5.9, NE)	1.0916 (0.4091, 2.9123) 0.8611	0.8638

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.3806
Normal Function	170	52 (30.6)	118 (69.4)	NE (18.3, NE)	98	30 (30.6)	68 (69.4)	11.7 (6.9, NE)	0.6506 (0.4116, 1.0286) 0.0659	0.0635	
Mild Impairment	195	55 (28.2)	140 (71.8)	21.7 (16.6, NE)	84	28 (33.3)	56 (66.7)	10.0 (4.9, NE)	0.4817 (0.2996, 0.7745) 0.0026	0.0021	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.0366
Yes	332	97 (29.2)	235 (70.8)	21.7 (17.6, NE)	157	46 (29.3)	111 (70.7)	11.7 (8.3, NE)	0.6404 (0.4475, 0.9165) 0.0148	0.0141	
No	41	11 (26.8)	30 (73.2)	NE (9.9, NE)	27	14 (51.9)	13 (48.1)	4.7 (2.8, NE)	0.2653 (0.1154, 0.6094) 0.0018	0.0009	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.2250
Positive	331	97 (29.3)	234 (70.7)	NE (18.3, NE)	163	51 (31.3)	112 (68.7)	10.2 (7.1, NE)	0.5994 (0.4239, 0.8476) 0.0038	0.0034	
Negative	42	11 (26.2)	31 (73.8)	NE (7.8, NE)	21	9 (42.9)	12 (57.1)	5.3 (1.7, NE)	0.2679 (0.1026, 0.6992) 0.0071	0.0044	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.9490
Positive	333	95 (28.5)	238 (71.5)	NE (18.3, NE)	166	54 (32.5)	112 (67.5)	10.2 (6.9, NE)	0.5632 (0.4002, 0.7926) 0.0010	0.0008	
Negative	40	13 (32.5)	27 (67.5)	17.6 (7.4, NE)	18	6 (33.3)	12 (66.7)	5.8 (1.7, NE)	0.3974 (0.1399, 1.1290) 0.0832	0.0744	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.2752
HER2 IHC 1+	214	92 (43.0)	122 (57.0)	13.3 (9.1, 23.0)	107	31 (29.0)	76 (71.0)	11.4 (9.5, NE)	1.1576 (0.7660, 1.7493) 0.4872	0.4982
HER2 IHC 2+/ISH Negative	159	68 (42.8)	91 (57.2)	18.2 (8.5, 27.2)	77	31 (40.3)	46 (59.7)	9.0 (5.1, NE)	0.8304 (0.5408, 1.2750) 0.3955	0.3890

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.3110
1	221	97 (43.9)	124 (56.1)	13.6 (8.5, 21.7)	100	32 (32.0)	68 (68.0)	11.3 (9.0, NE)	1.1640 (0.7780, 1.7415)	0.4690
>=2	151	63 (41.7)	88 (58.3)	13.3 (9.8, 27.2)	83	30 (36.1)	53 (63.9)	11.7 (5.9, NE)	0.8227 (0.5279, 1.2821)	0.3885

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.6603
Yes	235	100 (42.6)	135 (57.4)	13.6 (10.4, 22.3)	118	38 (32.2)	80 (67.8)	9.5 (6.2, NE)	0.9938 (0.6802, 1.4519) 0.9742	0.9628	
No	98	43 (43.9)	55 (56.1)	16.3 (8.3, 27.2)	48	19 (39.6)	29 (60.4)	11.3 (6.1, NE)	0.8680 (0.5030, 1.4979) 0.6112	0.6060	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8237
<65	290	123 (42.4)	167 (57.6)	18.2 (10.6, 23.0)	136	43 (31.6)	93 (68.4)	11.4 (6.2, NE)	1.0027 (0.7050, 1.4260) 0.9880	0.9993	
>=65	83	37 (44.6)	46 (55.4)	11.2 (4.9, NE)	48	19 (39.6)	29 (60.4)	10.5 (6.5, 14.4)	1.0106 (0.5781, 1.7666) 0.9705	0.9759	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7462
<75	359	153 (42.6)	206 (57.4)	16.3 (10.4, 22.3)	175	56 (32.0)	119 (68.0)	11.4 (8.5, NE)	1.0275 (0.7536, 1.4009) 0.8640	0.8777	
>=75	14	7 (50.0)	7 (50.0)	8.5 (1.6, NE)	9	6 (66.7)	3 (33.3)	11.3 (0.7, 14.4)	0.8677 (0.2887, 2.6082) 0.8005	0.8003	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.2551
White	176	65 (36.9)	111 (63.1)	21.7 (13.3, NE)	91	29 (31.9)	62 (68.1)	11.4 (5.1, NE)	0.8401 (0.5377, 1.3126) 0.4440	0.4387	
Non-White	197	95 (48.2)	102 (51.8)	10.4 (7.6, 18.2)	92	33 (35.9)	59 (64.1)	11.3 (8.5, NE)	1.1270 (0.7556, 1.6808) 0.5578	0.5691	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.4153
Asia	147	77 (52.4)	70 (47.6)	10.4 (7.5, 18.2)	66	24 (36.4)	42 (63.6)	11.3 (6.1, NE)	1.2349 (0.7778, 1.9606) 0.3710	0.3784	
North America	60	16 (26.7)	44 (73.3)	22.3 (22.3, NE)	33	6 (18.2)	27 (81.8)	11.4 (11.4, NE)	1.0211 (0.3919, 2.6600) 0.9660	0.9672	
Europe + Israel	166	67 (40.4)	99 (59.6)	18.3 (9.1, NE)	85	32 (37.6)	53 (62.4)	9.0 (5.1, NE)	0.8180 (0.5333, 1.2547) 0.3573	0.3507	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.1092
0	200	80 (40.0)	120 (60.0)	21.7 (12.0, 27.2)	105	36 (34.3)	69 (65.7)	11.4 (6.5, NE)	0.7859 (0.5271, 1.1718) 0.2371	0.2321	
1	173	80 (46.2)	93 (53.8)	8.4 (5.6, NE)	79	26 (32.9)	53 (67.1)	11.3 (6.2, NE)	1.3274 (0.8491, 2.0751) 0.2141	0.2188	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.5084
0	60	25 (41.7)	35 (58.3)	NE (3.1, NE)	34	11 (32.4)	23 (67.6)	NE (2.9, NE)	1.0545 (0.5175, 2.1487)	0.8838
1	108	49 (45.4)	59 (54.6)	11.8 (7.5, 21.7)	51	17 (33.3)	34 (66.7)	10.5 (8.5, NE)	1.2217 (0.6998, 2.1328)	0.4824
2	115	41 (35.7)	74 (64.3)	22.3 (12.5, NE)	54	18 (33.3)	36 (66.7)	11.4 (5.0, NE)	0.6683 (0.3770, 1.1845)	0.1621

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	45 (50.0)	45 (50.0)	11.2 (5.1, 23.0)	45	16 (35.6)	29 (64.4)	14.4 (4.4, NE)	1.1546 (0.6484, 2.0557) 0.6254	0.6337	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.3412
PD	174	70 (40.2)	104 (59.8)	13.6 (10.2, 27.2)	85	30 (35.3)	55 (64.7)	9.5 (5.1, NE)	0.8105 (0.5246, 1.2523) 0.3439	0.3382	
PR	48	26 (54.2)	22 (45.8)	10.1 (1.6, 22.3)	22	6 (27.3)	16 (72.7)	11.7 (3.1, NE)	1.6416 (0.6701, 4.0213) 0.2782	0.2788	
SD	82	27 (32.9)	55 (67.1)	NE (13.3, NE)	55	18 (32.7)	37 (67.3)	11.4 (6.5, NE)	0.8159 (0.4461, 1.4924) 0.5090	0.5051	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.6322
Yes	37	16 (43.2)	21 (56.8)	NE (1.5, NE)	15	3 (20.0)	12 (80.0)	NE (0.8, NE)	1.5400 (0.4474, 5.3003) 0.4935	0.4907	
No	336	144 (42.9)	192 (57.1)	13.6 (10.4, 22.3)	169	59 (34.9)	110 (65.1)	11.3 (8.5, NE)	0.9580 (0.7045, 1.3026) 0.7842	0.7726	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.1250
Yes	24	12 (50.0)	12 (50.0)	5.4 (1.4, NE)	8	1 (12.5)	7 (87.5)	NE (0.8, NE)	3.8843 (0.5048, 29.8884)	0.1604
No	349	148 (42.4)	201 (57.6)	13.6 (10.4, 22.3)	176	61 (34.7)	115 (65.3)	11.3 (7.5, NE)	0.9340 (0.6902, 1.2640)	0.6450

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.5597
Normal Function	202	83 (41.1)	119 (58.9)	18.2 (10.6, 22.3)	87	28 (32.2)	59 (67.8)	NE (5.1, NE)	0.9850 (0.6388, 1.5187) 0.9454	0.9288	
Mild Impairment	123	54 (43.9)	69 (56.1)	11.8 (7.6, NE)	69	24 (34.8)	45 (65.2)	11.4 (5.8, NE)	0.9373 (0.5740, 1.5307) 0.7959	0.7932	
Moderate Impairment	41	20 (48.8)	21 (51.2)	12.5 (4.2, NE)	23	8 (34.8)	15 (65.2)	14.4 (6.5, NE)	1.5352 (0.6744, 3.4949) 0.3071	0.3055	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1566
Normal Function	170	85 (50.0)	85 (50.0)	10.6 (6.2, 18.3)	98	33 (33.7)	65 (66.3)	11.7 (9.0, NE)	1.2216 (0.8142, 1.8327) 0.3336	0.3400	
Mild Impairment	195	72 (36.9)	123 (63.1)	21.7 (11.2, NE)	84	28 (33.3)	56 (66.7)	9.5 (5.0, NE)	0.8083 (0.5183, 1.2605) 0.3478	0.3407	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1206
Yes	332	144 (43.4)	188 (56.6)	13.3 (10.4, 21.7)	157	50 (31.8)	107 (68.2)	11.4 (8.5, NE)	1.0765 (0.7775, 1.4905) 0.6570	0.6693	
No	41	16 (39.0)	25 (61.0)	NE (4.9, NE)	27	12 (44.4)	15 (55.6)	9.0 (1.2, NE)	0.6796 (0.3165, 1.4593) 0.3218	0.3164	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.8813
Positive	331	143 (43.2)	188 (56.8)	13.6 (10.4, 22.3)	163	55 (33.7)	108 (66.3)	11.3 (8.5, NE)	0.9749 (0.7115, 1.3359) 0.8745	0.8604	
Negative	42	17 (40.5)	25 (59.5)	NE (2.9, NE)	21	7 (33.3)	14 (66.7)	NE (1.0, NE)	1.2086 (0.5000, 2.9213) 0.6740	0.6662	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.3859
Positive	333	142 (42.6)	191 (57.4)	16.3 (10.4, 22.3)	166	57 (34.3)	109 (65.7)	11.3 (8.5, NE)	0.9454 (0.6924, 1.2909) 0.7239	0.7098	
Negative	40	18 (45.0)	22 (55.0)	8.5 (2.9, NE)	18	5 (27.8)	13 (72.2)	NE (3.4, NE)	1.5704 (0.5785, 4.2632) 0.3758	0.3706	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.4716
HER2 IHC 1+	214	86 (40.2)	128 (59.8)	15.2 (11.5, NE)	107	31 (29.0)	76 (71.0)	NE (5.9, NE)	1.0439 (0.6889, 1.5820) 0.8394	0.8412	
HER2 IHC 2+/ISH Negative	159	69 (43.4)	90 (56.6)	11.1 (7.0, NE)	77	24 (31.2)	53 (68.8)	10.1 (6.7, NE)	1.2594 (0.7898, 2.0082) 0.3326	0.3359	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Number of prior lines of chemotherapy in a metastatic setting										0.5754
1	221	95 (43.0)	126 (57.0)	12.5 (8.5, NE)	100	34 (34.0)	66 (66.0)	11.3 (5.9, NE)	1.0305 (0.6942, 1.5295)	0.8816
>=2	151	59 (39.1)	92 (60.9)	16.6 (9.7, NE)	83	21 (25.3)	62 (74.7)	NE (7.5, NE)	1.2728 (0.7696, 2.1051)	0.3474

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.8619
Yes	235	96 (40.9)	139 (59.1)	12.5 (9.7, NE)	118	33 (28.0)	85 (72.0)	NE (6.7, NE)	1.0782 (0.7223, 1.6096) 0.7126	0.7190	
No	98	42 (42.9)	56 (57.1)	16.6 (6.8, NE)	48	17 (35.4)	31 (64.6)	11.3 (6.1, NE)	1.0864 (0.6173, 1.9122) 0.7738	0.7804	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4373
<65	290	123 (42.4)	167 (57.6)	14.0 (9.9, NE)	136	37 (27.2)	99 (72.8)	NE (6.1, NE)	1.2386 (0.8547, 1.7949) 0.2584	0.2639	
>=65	83	32 (38.6)	51 (61.4)	13.4 (5.8, NE)	48	18 (37.5)	30 (62.5)	8.4 (6.7, NE)	0.9168 (0.5126, 1.6399) 0.7698	0.7709	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Age											
<75	359	147 (40.9)	212 (59.1)	14.0 (11.3, NE)	175	52 (29.7)	123 (70.3)	NE (8.3, NE)	1.0813 (0.7855, 1.4885)	0.6408	0.1216
>=75	14	8 (57.1)	6 (42.9)	5.8 (1.4, NE)	9	3 (33.3)	6 (66.7)	11.3 (3.8, NE)	4.5256 (0.9519, 21.5169)	0.0380	

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.8310
White	176	73 (41.5)	103 (58.5)	11.5 (7.0, NE)	91	26 (28.6)	65 (71.4)	NE (5.8, NE)	1.1471 (0.7298, 1.8029) 0.5520	0.5560	
Non-White	197	82 (41.6)	115 (58.4)	14.5 (10.0, NE)	92	29 (31.5)	63 (68.5)	11.3 (8.3, NE)	1.0842 (0.7069, 1.6629) 0.7110	0.7185	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.4300
Asia	147	65 (44.2)	82 (55.8)	13.6 (9.0, NE)	66	21 (31.8)	45 (68.2)	11.3 (8.3, NE)	1.1973 (0.7296, 1.9649) 0.4761	0.4801	
North America	60	25 (41.7)	35 (58.3)	11.5 (4.3, 22.3)	33	6 (18.2)	27 (81.8)	NE (4.5, NE)	1.7202 (0.6938, 4.2651) 0.2417	0.2380	
Europe + Israel	166	65 (39.2)	101 (60.8)	14.5 (8.5, NE)	85	28 (32.9)	57 (67.1)	8.4 (5.9, NE)	0.9425 (0.6027, 1.4739) 0.7953	0.7915	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.3677
0	200	86 (43.0)	114 (57.0)	14.0 (8.7, NE)	105	26 (24.8)	79 (75.2)	NE (8.4, NE)	1.3284 (0.8543, 2.0657) 0.2074	0.2069	
1	173	69 (39.9)	104 (60.1)	13.6 (9.0, NE)	79	29 (36.7)	50 (63.3)	9.2 (5.9, NE)	0.9461 (0.6095, 1.4686) 0.8050	0.7922	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.7353
0	60	28 (46.7)	32 (53.3)	8.1 (1.6, NE)	34	10 (29.4)	24 (70.6)	NE (4.7, NE)	1.4930 (0.7234, 3.0811) 0.2783	0.2775	
1	108	42 (38.9)	66 (61.1)	11.5 (7.1, NE)	51	17 (33.3)	34 (66.7)	NE (5.8, NE)	1.1092 (0.6308, 1.9505) 0.7190	0.7218	
2	115	52 (45.2)	63 (54.8)	13.6 (8.7, NE)	54	14 (25.9)	40 (74.1)	NE (6.7, NE)	1.1861 (0.6493, 2.1667) 0.5788	0.5793	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	33 (36.7)	57 (63.3)	NE (9.9, NE)	45	14 (31.1)	31 (68.9)	9.2 (5.9, NE)	0.8934 (0.4734, 1.6861) 0.7279	0.7179

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.7318
PD	174	65 (37.4)	109 (62.6)	14.5 (9.9, NE)	85	22 (25.9)	63 (74.1)	NE (7.5, NE)	1.1213 (0.6888, 1.8254) 0.6452	0.6473
PR	48	18 (37.5)	30 (62.5)	22.3 (8.1, NE)	22	7 (31.8)	15 (68.2)	6.7 (4.7, NE)	0.7488 (0.3070, 1.8261) 0.5248	0.5170
SD	82	36 (43.9)	46 (56.1)	12.5 (7.0, NE)	55	18 (32.7)	37 (67.3)	11.3 (6.1, NE)	1.1293 (0.6379, 1.9994) 0.6764	0.6811

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.0899
Yes	37	14 (37.8)	23 (62.2)	NE (4.2, NE)	15	1 (6.7)	14 (93.3)	NE (5.9, NE)	4.5902 (0.6013, 35.0404)	0.1064
No	336	141 (42.0)	195 (58.0)	13.6 (10.0, NE)	169	54 (32.0)	115 (68.0)	11.3 (7.5, NE)	1.0651 (0.7760, 1.4619)	0.7068

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.3851
Yes	24	8 (33.3)	16 (66.7)	NE (4.2, NE)	8	1 (12.5)	7 (87.5)	NE (5.9, NE)	2.5821 (0.3206, 20.7964) 0.3728	0.3551	
No	349	147 (42.1)	202 (57.9)	13.6 (10.0, NE)	176	54 (30.7)	122 (69.3)	11.3 (8.3, NE)	1.1071 (0.8081, 1.5167) 0.5265	0.5350	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Renal function at baseline										0.2890
Normal Function	202	90 (44.6)	112 (55.4)	13.4 (8.1, NE)	87	26 (29.9)	61 (70.1)	10.1 (5.9, NE)	1.1417 (0.7345, 1.7746)	0.5640
Mild Impairment	123	48 (39.0)	75 (61.0)	NE (8.1, NE)	69	23 (33.3)	46 (66.7)	8.3 (5.8, NE)	0.9255 (0.5591, 1.5321)	0.7565
Moderate Impairment	41	17 (41.5)	24 (58.5)	15.2 (5.8, NE)	23	5 (21.7)	18 (78.3)	NE (11.3, NE)	2.1957 (0.8081, 5.9660)	0.1140

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.9840
Normal Function	170	77 (45.3)	93 (54.7)	13.4 (8.1, NE)	98	32 (32.7)	66 (67.3)	NE (7.5, NE)	1.1208 (0.7393, 1.6992) 0.5912	0.5956	
Mild Impairment	195	77 (39.5)	118 (60.5)	14.0 (9.8, NE)	84	23 (27.4)	61 (72.6)	11.3 (5.8, NE)	1.1568 (0.7230, 1.8510) 0.5435	0.5471	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1852
Yes	332	138 (41.6)	194 (58.4)	13.4 (9.9, NE)	157	43 (27.4)	114 (72.6)	NE (9.2, NE)	1.2390 (0.8777, 1.7491) 0.2232	0.2252	
No	41	17 (41.5)	24 (58.5)	14.5 (5.1, NE)	27	12 (44.4)	15 (55.6)	5.9 (4.4, NE)	0.7170 (0.3364, 1.5279) 0.3887	0.3810	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.8034
Positive	331	138 (41.7)	193 (58.3)	14.0 (10.1, NE)	163	47 (28.8)	116 (71.2)	NE (8.4, NE)	1.1444 (0.8197, 1.5977) 0.4282	0.4332	
Negative	42	17 (40.5)	25 (59.5)	12.3 (1.6, NE)	21	8 (38.1)	13 (61.9)	5.9 (4.4, NE)	1.0972 (0.4687, 2.5681) 0.8308	0.8384	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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## Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.4282
Positive	333	136 (40.8)	197 (59.2)	14.0 (11.1, NE)	166	50 (30.1)	116 (69.9)	11.3 (8.3, NE)	1.0768 (0.7765, 1.4932) 0.6575	0.6652	
Negative	40	19 (47.5)	21 (52.5)	9.8 (1.5, NE)	18	5 (27.8)	13 (72.2)	NE (5.8, NE)	1.6683 (0.6168, 4.5127) 0.3134	0.3073	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.9034
HER2 IHC 1+	214	55 (25.7)	159 (74.3)	NE (NE, NE)	107	19 (17.8)	88 (82.2)	NE (11.4, NE)	1.0443 (0.6147, 1.7741) 0.8728	0.8772
HER2 IHC 2+/ISH Negative	159	46 (28.9)	113 (71.1)	NE (16.8, NE)	77	17 (22.1)	60 (77.9)	14.4 (9.0, NE)	1.0162 (0.5789, 1.7839) 0.9554	0.9651

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.2200
1	221	66 (29.9)	155 (70.1)	NE (18.0, NE)	100	18 (18.0)	82 (82.0)	NE (11.4, NE)	1.2297 (0.7252, 2.0851) 0.4429	0.4446
>=2	151	35 (23.2)	116 (76.8)	NE (NE, NE)	83	18 (21.7)	65 (78.3)	14.4 (9.0, NE)	0.8305 (0.4669, 1.4774) 0.5274	0.5167

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.5219
Yes	235	68 (28.9)	167 (71.1)	NE (18.0, NE)	118	22 (18.6)	96 (81.4)	NE (9.2, NE)	1.1091 (0.6807, 1.8072) 0.6776	0.6786	
No	98	21 (21.4)	77 (78.6)	NE (NE, NE)	48	9 (18.8)	39 (81.3)	NE (11.4, NE)	0.8239 (0.3720, 1.8249) 0.6331	0.6242	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9446
<65	290	80 (27.6)	210 (72.4)	NE (21.7, NE)	136	26 (19.1)	110 (80.9)	NE (9.3, NE)	1.0139 (0.6468, 1.5892) 0.9522	0.9627	
>=65	83	21 (25.3)	62 (74.7)	NE (NE, NE)	48	10 (20.8)	38 (79.2)	14.4 (11.4, NE)	1.0352 (0.4814, 2.2261) 0.9294	0.9279	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3930
<75	359	94 (26.2)	265 (73.8)	NE (21.7, NE)	175	33 (18.9)	142 (81.1)	NE (11.4, NE)	1.0095 (0.6747, 1.5104) 0.9633	0.9733	
>=75	14	7 (50.0)	7 (50.0)	14.1 (1.6, NE)	9	3 (33.3)	6 (66.7)	14.4 (0.8, 14.4)	1.7818 (0.4531, 7.0072) 0.4084	0.4021	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.2200
White	176	57 (32.4)	119 (67.6)	21.7 (14.1, NE)	91	17 (18.7)	74 (81.3)	NE (9.2, NE)	1.3375 (0.7716, 2.3182) 0.3001	0.3012	
Non-White	197	44 (22.3)	153 (77.7)	NE (NE, NE)	92	19 (20.7)	73 (79.3)	14.4 (9.5, NE)	0.7827 (0.4536, 1.3504) 0.3786	0.3723	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.2715
Asia	147	32 (21.8)	115 (78.2)	NE (NE, NE)	66	15 (22.7)	51 (77.3)	14.4 (9.3, NE)	0.6945 (0.3734, 1.2918) 0.2496	0.2436	
North America	60	17 (28.3)	43 (71.7)	NE (9.1, NE)	33	6 (18.2)	27 (81.8)	13.3 (NE, NE)	0.9692 (0.3710, 2.5320) 0.9490	0.9528	
Europe + Israel	166	52 (31.3)	114 (68.7)	21.7 (16.8, NE)	85	15 (17.6)	70 (82.4)	NE (9.5, NE)	1.4408 (0.8043, 2.5811) 0.2195	0.2201	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	200	58 (29.0)	142 (71.0)	NE (18.0, NE)	105	22 (21.0)	83 (79.0)	NE (9.5, NE)	0.9390 (0.5702, 1.5463) 0.8047	0.8005	0.6017
1	173	43 (24.9)	130 (75.1)	NE (NE, NE)	79	14 (17.7)	65 (82.3)	NE (9.2, NE)	1.1760 (0.6389, 2.1646) 0.6026	0.6104	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1439
0	60	18 (30.0)	42 (70.0)	16.8 (12.5, NE)	34	6 (17.6)	28 (82.4)	NE (9.0, NE)	1.2112 (0.4747, 3.0905) 0.6885	0.6908	
1	108	29 (26.9)	79 (73.1)	NE (21.7, NE)	51	10 (19.6)	41 (80.4)	NE (9.5, NE)	1.1745 (0.5683, 2.4273) 0.6641	0.6681	
2	115	32 (27.8)	83 (72.2)	NE (14.3, NE)	54	6 (11.1)	48 (88.9)	NE (NE, NE)	1.7953 (0.7403, 4.3540) 0.1954	0.1907	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	22 (24.4)	68 (75.6)	NE (18.0, NE)	45	14 (31.1)	31 (68.9)	9.3 (8.6, NE)	0.5279 (0.2655, 1.0496) 0.0685	0.0641	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.4907
PD	174	53 (30.5)	121 (69.5)	NE (13.5, NE)	85	13 (15.3)	72 (84.7)	NE (9.5, NE)	1.5436 (0.8348, 2.8543) 0.1663	0.1658	
PR	48	11 (22.9)	37 (77.1)	NE (NE, NE)	22	4 (18.2)	18 (81.8)	NE (8.6, NE)	0.7722 (0.2405, 2.4791) 0.6640	0.6558	
SD	82	24 (29.3)	58 (70.7)	NE (16.8, NE)	55	12 (21.8)	43 (78.2)	NE (9.0, NE)	1.1400 (0.5662, 2.2953) 0.7137	0.7111	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.0107
Yes	37	13 (35.1)	24 (64.9)	16.1 (5.9, NE)	15	0	15 (100)	NE (NE, NE)	NE (NE, NE) 0.9935	0.0721	
No	336	88 (26.2)	248 (73.8)	NE (21.7, NE)	169	36 (21.3)	133 (78.7)	14.4 (11.4, NE)	0.9249 (0.6237, 1.3715) 0.6977	0.6871	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0794
Yes	24	7 (29.2)	17 (70.8)	NE (5.9, NE)	8	0	8 (100)	NE (NE, NE)	NE (NE, NE) 0.9956	0.2366	
No	349	94 (26.9)	255 (73.1)	NE (21.7, NE)	176	36 (20.5)	140 (79.5)	14.4 (11.4, NE)	0.9882 (0.6690, 1.4598) 0.9526	0.9415	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Renal function at baseline										0.3489
Normal Function	202	56 (27.7)	146 (72.3)	NE (16.8, NE)	87	12 (13.8)	75 (86.2)	NE (13.3, NE)	1.4015 (0.7453, 2.6351) 0.2948	0.2972
Mild Impairment	123	35 (28.5)	88 (71.5)	NE (18.0, NE)	69	16 (23.2)	53 (76.8)	NE (9.0, NE)	0.8951 (0.4879, 1.6423) 0.7205	0.7197
Moderate Impairment	41	9 (22.0)	32 (78.0)	NE (13.5, NE)	23	7 (30.4)	16 (69.6)	14.4 (9.5, NE)	0.7409 (0.2749, 1.9970) 0.5534	0.5523

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.7064
Normal Function	170	54 (31.8)	116 (68.2)	NE (16.8, NE)	98	21 (21.4)	77 (78.6)	NE (11.4, NE)	1.0943 (0.6563, 1.8244) 0.7298	0.7339
Mild Impairment	195	46 (23.6)	149 (76.4)	NE (21.7, NE)	84	15 (17.9)	69 (82.1)	13.3 (9.3, NE)	0.9515 (0.5258, 1.7216) 0.8694	0.8659

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1681
Yes	332	90 (27.1)	242 (72.9)	NE (21.7, NE)	157	27 (17.2)	130 (82.8)	NE (11.4, NE)	1.1611 (0.7512, 1.7946) 0.5014	0.5041	
No	41	11 (26.8)	30 (73.2)	NE (16.8, NE)	27	9 (33.3)	18 (66.7)	9.0 (5.3, NE)	0.6516 (0.2618, 1.6215) 0.3571	0.3448	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (IXRS)										0.9649
Positive	331	89 (26.9)	242 (73.1)	NE (21.7, NE)	163	31 (19.0)	132 (81.0)	NE (11.4, NE)	1.0315 (0.6816, 1.5611)	0.8873
Negative	42	12 (28.6)	30 (71.4)	NE (7.8, NE)	21	5 (23.8)	16 (76.2)	9.0 (5.3, NE)	0.9989 (0.3424, 2.9139)	0.9886

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (derived)										0.7022
Positive	333	89 (26.7)	244 (73.3)	NE (21.7, NE)	166	31 (18.7)	135 (81.3)	NE (11.4, NE)	1.0564 (0.6980, 1.5989) 0.7952	0.8006
Negative	40	12 (30.0)	28 (70.0)	NE (7.8, NE)	18	5 (27.8)	13 (72.2)	9.0 (5.3, NE)	0.8226 (0.2813, 2.4051) 0.7212	0.7127

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status									0.9682
HER2 IHC 1+	214	47 (22.0)	167 (78.0)	107	25 (23.4)	82 (76.6)	18.5 (11.3, 18.5)	0.5899 (0.3575, 0.9733) 0.0389	0.0366
HER2 IHC 2+/ISH Negative	159	32 (20.1)	127 (79.9)	77	17 (22.1)	60 (77.9)	17.5 (17.5, NE)	0.5925 (0.3247, 1.0812) 0.0881	0.0848

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.6533
1	221	46 (20.8)	175 (79.2)	NE (NE, NE)	100	23 (23.0)	77 (77.0)	17.5 (11.3, NE)	0.6693 (0.4024, 1.1133)	0.1192
>=2	151	32 (21.2)	119 (78.8)	28.1 (NE, NE)	83	19 (22.9)	64 (77.1)	18.5 (6.9, 18.5)	0.4751 (0.2621, 0.8615)	0.0123

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Prior CDK4/6										0.6891
Yes	235	50 (21.3)	185 (78.7)	NE (20.9, NE)	118	24 (20.3)	94 (79.7)	18.5 (18.5, NE)	0.6861 (0.4173, 1.1279) 0.1375	0.1359
No	98	21 (21.4)	77 (78.6)	NE (NE, NE)	48	12 (25.0)	36 (75.0)	17.5 (8.6, NE)	0.5402 (0.2605, 1.1203) 0.0980	0.0923

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Age										0.3228
<65	290	61 (21.0)	229 (79.0)	NE (NE, NE)	136	33 (24.3)	103 (75.7)	17.5 (17.5, NE)	0.5464 (0.3543, 0.8428) 0.0063	0.0055
>=65	83	18 (21.7)	65 (78.3)	28.1 (17.8, NE)	48	9 (18.8)	39 (81.3)	18.5 (8.6, 18.5)	0.6914 (0.2980, 1.6040) 0.3900	0.3868

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Age										0.3558
<75	359	74 (20.6)	285 (79.4)	28.1 (28.1, NE)	175	39 (22.3)	136 (77.7)	18.5 (17.5, NE)	0.5730 (0.3845, 0.8541) 0.0063	0.0056
>=75	14	5 (35.7)	9 (64.3)	17.8 (1.6, 17.8)	9	3 (33.3)	6 (66.7)	11.3 (3.5, NE)	0.9579 (0.2118, 4.3324) 0.9555	0.9556

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.8889
White	176	38 (21.6)	138 (78.4)	NE (20.9, NE)	91	20 (22.0)	71 (78.0)	18.5 (NE, NE)	0.6635 (0.3801, 1.1581) 0.1489	0.1453	
Non-White	197	41 (20.8)	156 (79.2)	28.1 (28.1, NE)	92	22 (23.9)	70 (76.1)	17.5 (11.3, NE)	0.5241 (0.3073, 0.8938) 0.0177	0.0160	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Region										0.9031
Asia	147	33 (22.4)	114 (77.6)	28.1 (28.1, NE)	66	18 (27.3)	48 (72.7)	17.5 (11.3, NE)	0.4764 (0.2633, 0.8620) 0.0142	0.0123
North America	60	10 (16.7)	50 (83.3)	NE (20.9, NE)	33	5 (15.2)	28 (84.8)	NE (4.4, NE)	0.7879 (0.2616, 2.3732) 0.6718	0.6720
Europe + Israel	166	36 (21.7)	130 (78.3)	NE (NE, NE)	85	19 (22.4)	66 (77.6)	18.5 (NE, NE)	0.6723 (0.3803, 1.1885) 0.1719	0.1681

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	200	45 (22.5)	155 (77.5)	28.1 (20.9, NE)	105	21 (20.0)	84 (80.0)	18.5 (17.5, NE)	0.6918 (0.4073, 1.1750) 0.1728	0.1707	0.4035
1	173	34 (19.7)	139 (80.3)	NE (NE, NE)	79	21 (26.6)	58 (73.4)	11.3 (7.0, NE)	0.4679 (0.2648, 0.8268) 0.0089	0.0075	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.1952
0	60	12 (20.0)	48 (80.0)	NE (17.8, NE)	34	9 (26.5)	25 (73.5)	17.5 (5.9, 17.5)	0.3505 (0.1396, 0.8798)	0.0204
1	108	21 (19.4)	87 (80.6)	NE (15.9, NE)	51	11 (21.6)	40 (78.4)	18.5 (11.3, 18.5)	0.6693 (0.3179, 1.4089)	0.2872
2	115	22 (19.1)	93 (80.9)	NE (NE, NE)	54	15 (27.8)	39 (72.2)	NE (6.7, NE)	0.4031 (0.2028, 0.8014)	0.0074

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	24 (26.7)	66 (73.3)	28.1 (28.1, NE)	45	7 (15.6)	38 (84.4)	NE (NE, NE)	1.1454 (0.4839, 2.7112) 0.7574	0.7591

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.9928
PD	174	35 (20.1)	139 (79.9)	28.1 (NE, NE)	85	20 (23.5)	65 (76.5)	18.5 (8.6, 18.5)	0.5878 (0.3341, 1.0342)	0.0616
PR	48	12 (25.0)	36 (75.0)	NE (17.8, NE)	22	5 (22.7)	17 (77.3)	NE (6.7, NE)	0.5727 (0.1936, 1.6945)	0.3121
SD	82	19 (23.2)	63 (76.8)	NE (15.9, NE)	55	14 (25.5)	41 (74.5)	17.5 (11.3, NE)	0.5344 (0.2621, 1.0898)	0.0809

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Reported history of CNS metastases										0.2046
Yes	37	8 (21.6)	29 (78.4)	20.9 (20.9, NE)	15	1 (6.7)	14 (93.3)	NE (NE, NE)	2.0858 (0.2529, 17.1989)	0.4850
No	336	71 (21.1)	265 (78.9)	28.1 (28.1, NE)	169	41 (24.3)	128 (75.7)	17.5 (11.3, NE)	0.5471 (0.3681, 0.8131)	0.0025

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 15SEP2022 – 12:07; Program name: T3\_EQ5D\_FD\_2\_FAS.sas; Output name: T3\_EORTCC30\_DD\_2\_FAS.rtf

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0894
Yes	24	4 (16.7)	20 (83.3)	16.5 (16.5, NE)	8	0	8 (100)	NE (NE, NE)	NE (NE, NE) 0.9962	0.2697	
No	349	75 (21.5)	274 (78.5)	28.1 (28.1, NE)	176	42 (23.9)	134 (76.1)	17.5 (11.3, NE)	0.5656 (0.3833, 0.8348) 0.0041	0.0037	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 15SEP2022 – 12:07; Program name: T3\_EQ5D\_FD\_2\_FAS.sas; Output name: T3\_EORTCC30\_DD\_2\_FAS.rtf

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]	
Renal function at baseline										0.2219	
Normal Function	202	47 (23.3)	155 (76.7)	NE (20.9, NE)	87	21 (24.1)	66 (75.9)	17.5 (8.6, NE)	0.6450 (0.3821, 1.0886)	0.1006	0.0974
Mild Impairment	123	21 (17.1)	102 (82.9)	28.1 (NE, NE)	69	16 (23.2)	53 (76.8)	NE (8.4, NE)	0.3473 (0.1700, 0.7094)	0.0037	0.0026
Moderate Impairment	41	10 (24.4)	31 (75.6)	NE (11.2, NE)	23	5 (21.7)	18 (78.3)	18.5 (11.3, 18.5)	0.9970 (0.3375, 2.9452)	0.9957	0.9957

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 15SEP2022 – 12:07; Program name: T3\_EQ5D\_FD\_2\_FAS.sas; Output name: T3\_EORTCC30\_DD\_2\_FAS.rtf

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Hepatic function at baseline										0.3668
Normal Function	170	39 (22.9)	131 (77.1)	28.1 (20.9, NE)	98	27 (27.6)	71 (72.4)	17.5 (8.6, NE)	0.5258 (0.3169, 0.8724) 0.0128	0.0115
Mild Impairment	195	40 (20.5)	155 (79.5)	NE (NE, NE)	84	15 (17.9)	69 (82.1)	18.5 (11.3, 18.5)	0.6947 (0.3776, 1.2780) 0.2415	0.2381

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Baseline visceral disease										0.1147
Yes	332	69 (20.8)	263 (79.2)	NE (NE, NE)	157	32 (20.4)	125 (79.6)	17.5 (17.5, NE)	0.6818 (0.4444, 1.0461)	0.0775
No	41	10 (24.4)	31 (75.6)	28.1 (13.1, 28.1)	27	10 (37.0)	17 (63.0)	6.7 (4.4, NE)	0.2700 (0.1031, 0.7067)	0.0047

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (IXRS)										0.4134
Positive	331	69 (20.8)	262 (79.2)	NE (NE, NE)	163	35 (21.5)	128 (78.5)	17.5 (17.5, NE)	0.6263 (0.4130, 0.9497)	0.0263
Negative	42	10 (23.8)	32 (76.2)	28.1 (8.8, 28.1)	21	7 (33.3)	14 (66.7)	7.0 (4.4, NE)	0.3736 (0.1305, 1.0694)	0.0561

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (derived)										0.3390
Positive	333	70 (21.0)	263 (79.0)	NE (NE, NE)	166	36 (21.7)	130 (78.3)	17.5 (11.3, NE)	0.6291 (0.4167, 0.9496)	0.0260
Negative	40	9 (22.5)	31 (77.5)	28.1 (17.8, 28.1)	18	6 (33.3)	12 (66.7)	7.0 (1.7, NE)	0.3092 (0.1002, 0.9542)	0.0318

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

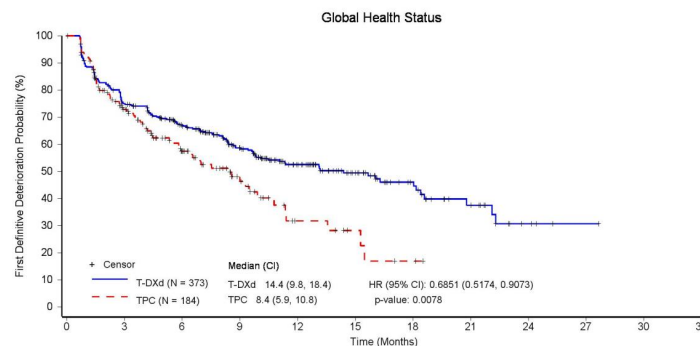
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Patients still at risk:

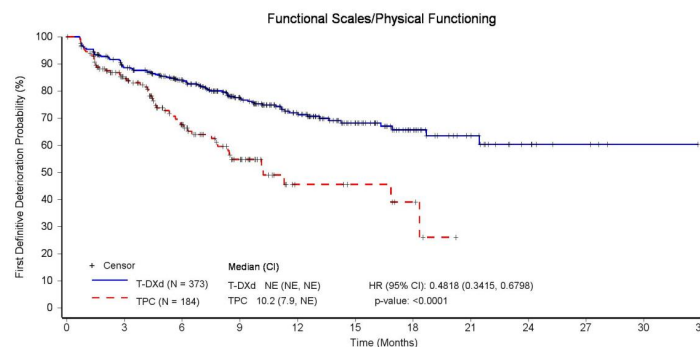
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	251	195	139	83	54	31	16	4	1	0	0
TPC (N = 184)	184	99	54	27	9	5	2	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	291	238	177	113	71	40	22	8	4	1	0
TPC (N = 184)	184	114	62	31	9	7	4	0	0	0	0	0

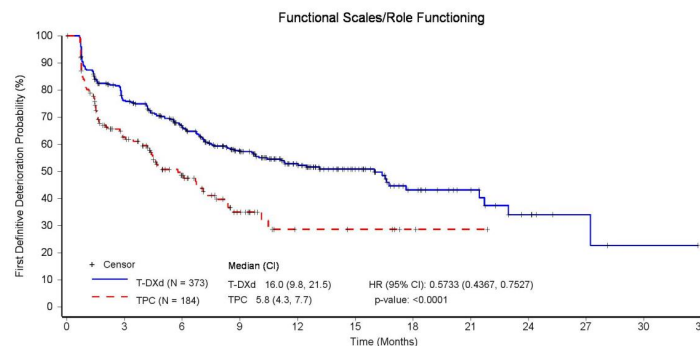
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	251	193	137	85	51	28	17	7	3	1	0
TPC (N = 184)	184	83	45	19	6	5	2	1	0	0	0	0

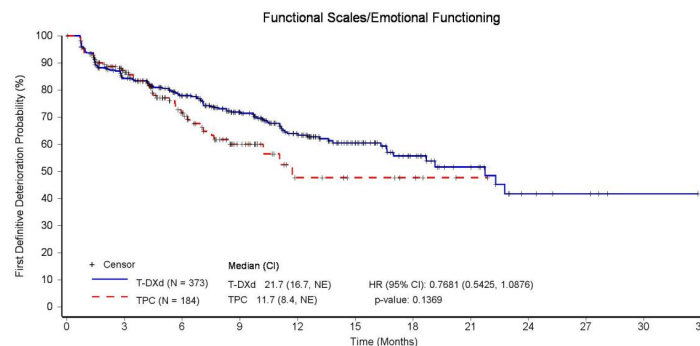
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

T-DXd (N = 373)	373	280	226	168	109	67	38	20	6	4	1	0
TPC (N = 184)	184	115	61	27	9	6	4	1	0	0	0	0

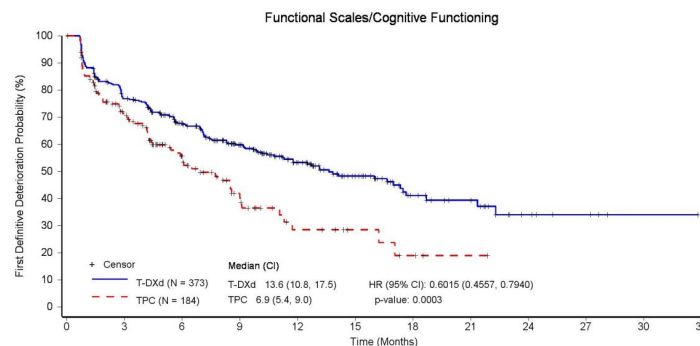
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

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Patients still at risk:

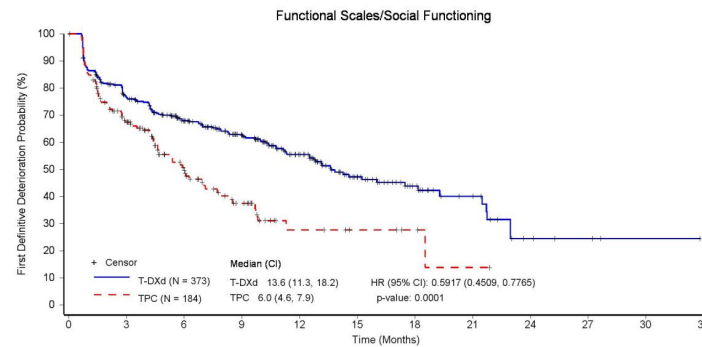
T-DXd (N = 373)	373	252	191	138	90	55	29	18	7	4	1	0
TPC (N = 184)	184	99	50	24	10	6	3	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:15; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F3\_EORTCC30\_DD\_3\_FAS.rf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	251	191	146	92	50	29	16	5	3	1	0
TPC (N = 184)	184	97	50	25	8	5	3	1	0	0	0	0

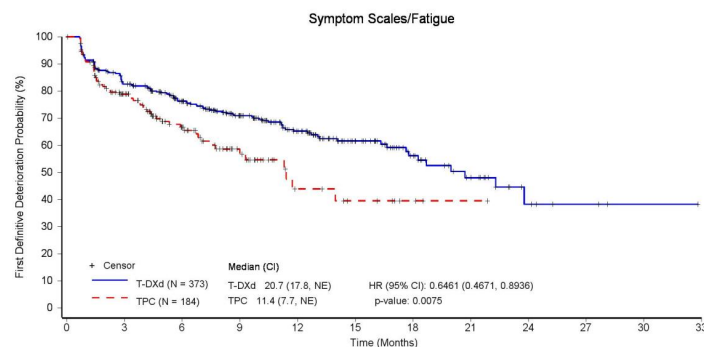
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

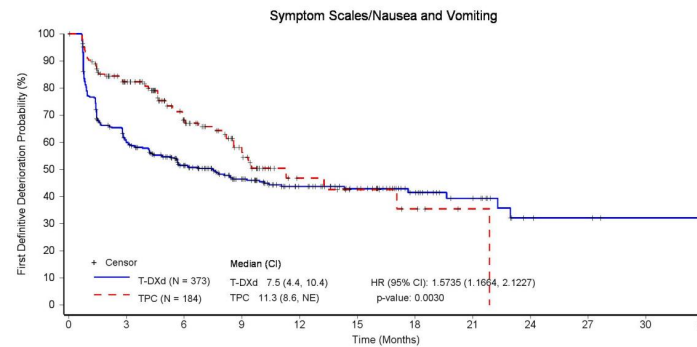
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	272	214	166	108	64	36	20	6	3	1	0
TPC (N = 184)	184	105	59	30	11	7	3	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 DE.F.3.6.3 - EORTC QLQ-C30 - Definitive deterioration - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	198	141	97	65	48	28	17	4	3	1	0
TPC (N = 184)	184	111	62	32	11	7	4	1	0	0	0	0

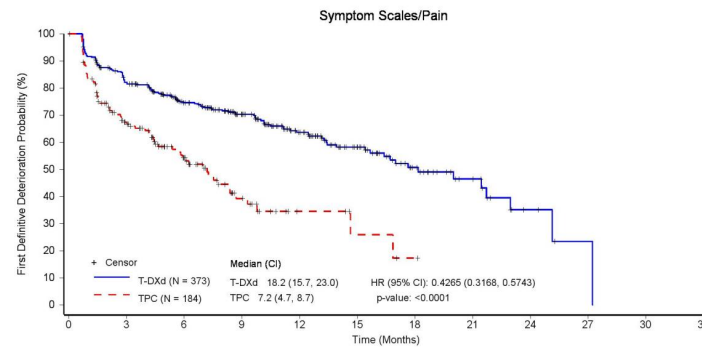
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:15; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F3\_EORTCC30\_DD\_3\_FAS.rf



Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
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Patients still at risk:

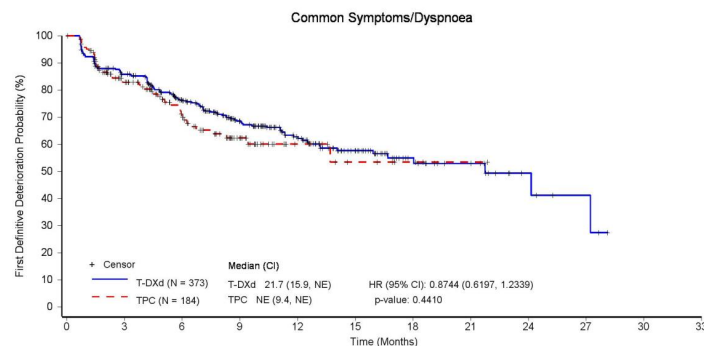
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	271	208	159	99	59	32	16	4	1	0	0
TPC (N = 184)	184	91	49	20	6	3	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:15; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F3\_EORTCC30\_DD\_3\_FAS.rtf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.3.6.3 - EORTC QLQ-C30 - Definitive deterioration - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	282	214	152	101	59	27	18	6	3	0	0
TPC (N = 184)	184	108	63	32	11	6	3	1	0	0	0	0

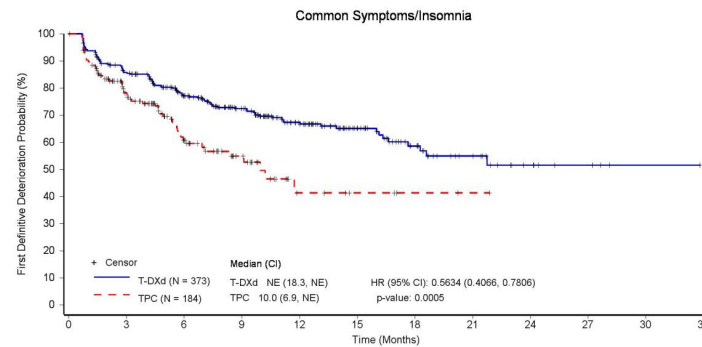
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:15; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F3\_EORTCC30\_DD\_3\_FAS.rf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)

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DE.F.3.6.3 - EORTC QLQ-C30 - Definitive deterioration - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

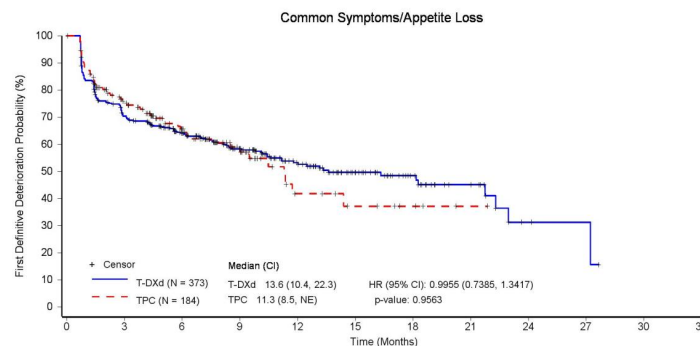
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	282	213	161	106	64	36	20	8	4	1	0
TPC (N = 184)	184	103	52	26	7	4	2	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:15; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F3\_EORTCC30\_DD\_3\_FAS.rf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	237	183	137	86	50	30	15	3	2	0	0
TPC (N = 184)	184	103	59	32	11	7	4	1	0	0	0	0

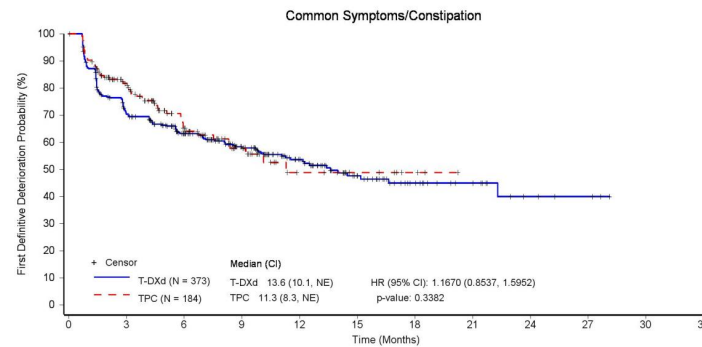
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:15; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F3\_EORTCC30\_DD\_3\_FAS.rf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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DE.F.3.6.3 - EORTC QLQ-C30 - Definitive deterioration - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

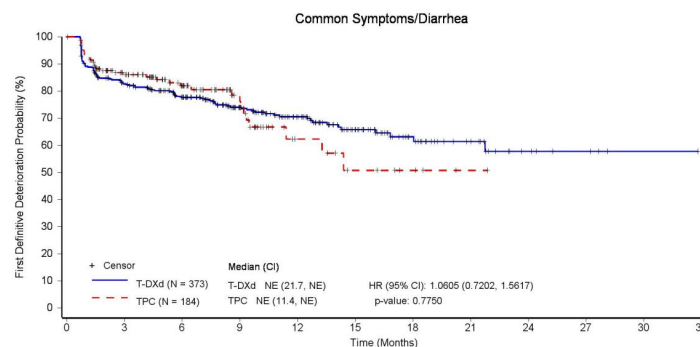
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	232	175	129	78	42	24	14	5	3	0	0
TPC (N = 184)	184	107	58	28	11	7	3	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:15; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F3\_EORTCC30\_DD\_3\_FAS.rf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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Patients still at risk:

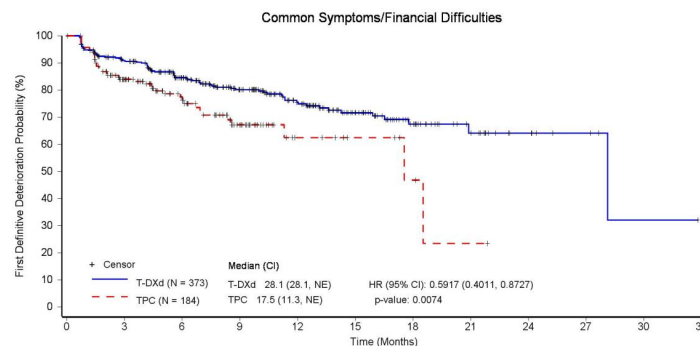
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	269	219	162	109	65	36	21	7	4	1	0
TPC (N = 184)	184	112	66	35	12	7	4	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:15; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F3\_EORTCC30\_DD\_3\_FAS.rf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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Patients still at risk:

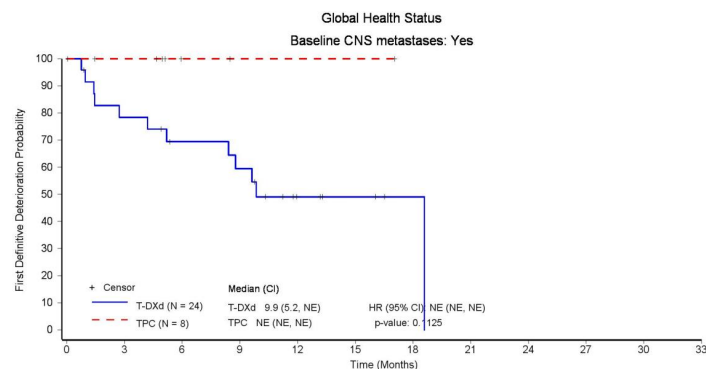
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	292	230	173	115	70	39	19	8	4	1	0
TPC (N = 184)	184	112	64	32	10	6	3	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:15; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F3\_EORTCC30\_DD\_3\_FAS.rf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 24)	24	18	14	12	5	3	1	0	0	0	0	0
TPC (N = 8)	8	6	2	1	1	1	0	0	0	0	0	0

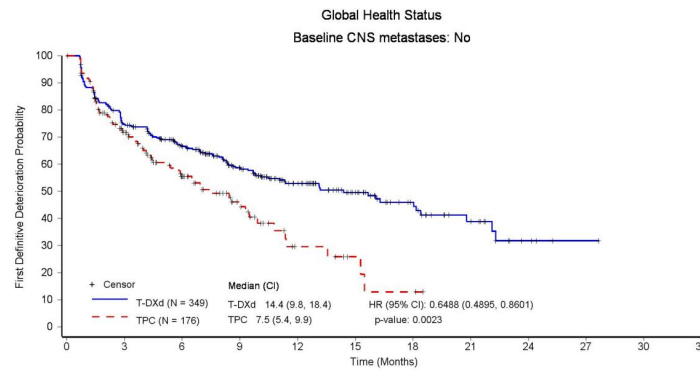
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:16; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_DD\_4\_FAS.rf



Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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Patients still at risk:

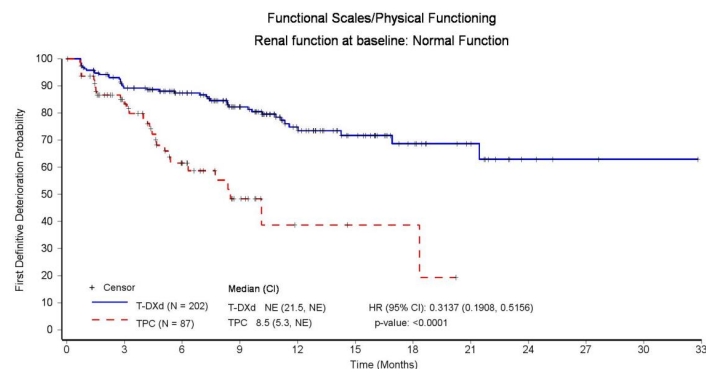
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 349)	349	233	181	127	78	51	30	16	4	1	0	0
TPC (N = 176)	176	93	52	26	8	4	2	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:16; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_DD\_4\_FAS.rf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.3.6.4 - EORTC QLQ-C30 - Definitive deterioration - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

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Patients still at risk:

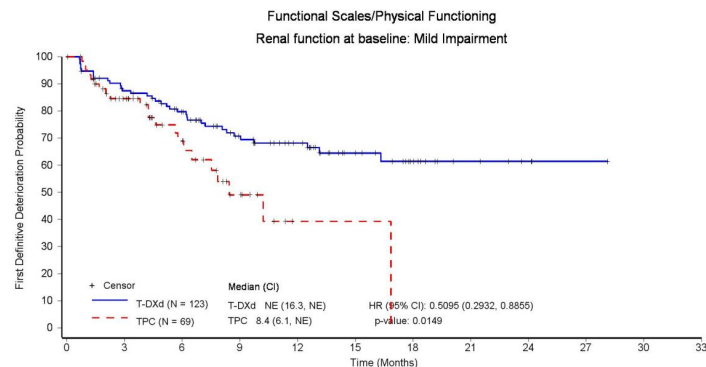
T-DXd (N = 202)	202	160	131	97	56	37	21	13	4	2	1	0
TPC (N = 87)	87	49	25	11	3	2	2	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:16; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_DD\_4\_FAS.rf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.3.6.4 - EORTC QLQ-C30 - Definitive deterioration - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

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Patients still at risk:

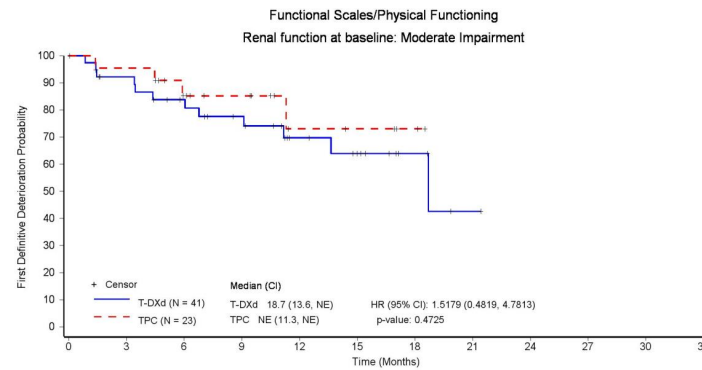
T-DXd (N = 123)	123	94	78	56	42	24	14	7	3	1	0	0
TPC (N = 69)	69	42	23	9	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:16; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_DD\_4\_FAS.rf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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Patients still at risk:

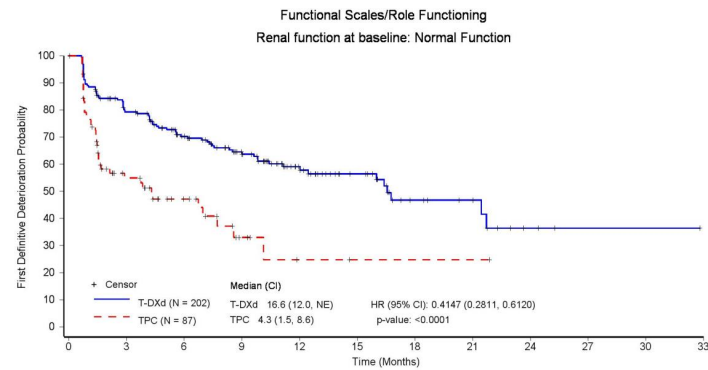
T-DXd (N = 41)	41	33	27	22	13	9	4	1	0	0	0	0
TPC (N = 23)	23	21	14	11	5	4	2	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:16; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_DD\_4\_FAS.rf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.3.6.4 - EORTC QLQ-C30 - Definitive deterioration - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

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Patients still at risk:

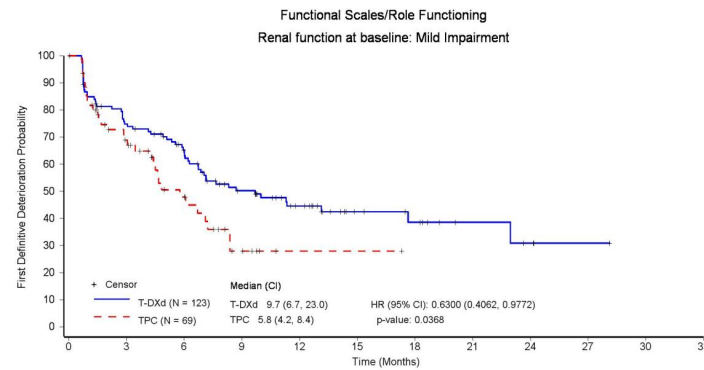
T-DXd (N = 202)	202	141	107	79	46	30	14	10	3	1	1	0
TPC (N = 87)	87	31	17	6	2	1	1	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:16; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_DD\_4\_FAS.rf

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Patients still at risk:

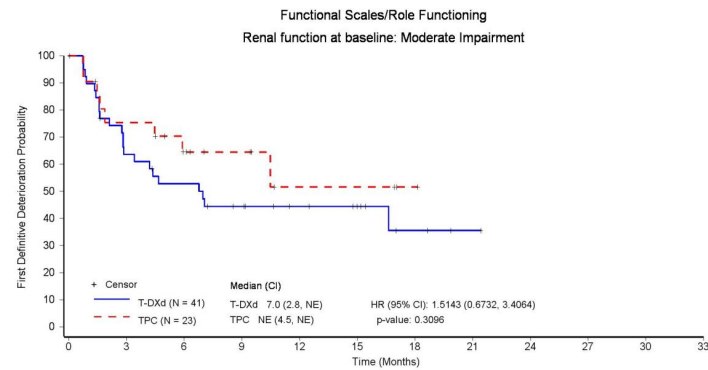
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 123)	123	81	64	41	27	13	10	5	3	1	0	0
TPC (N = 69)	69	35	18	6	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

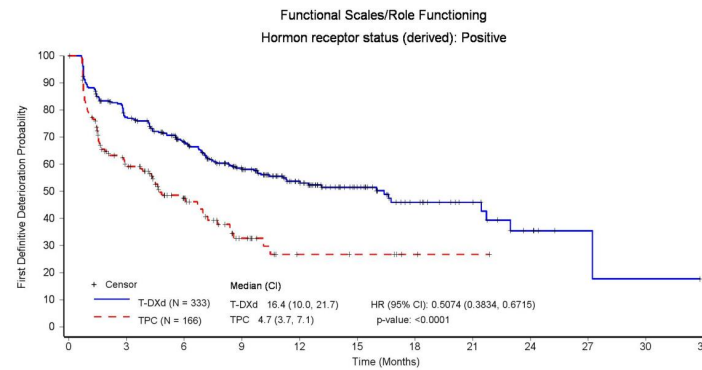
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 41)	41	24	19	14	10	7	3	1	0	0	0	0
TPC (N = 23)	23	15	10	7	3	3	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:16; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_DD\_4\_FAS.rf

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 Data Intelligence – Evidence Generation  
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 DE.F.3.6.4 - EORTC QLQ-C30 - Definitive deterioration - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 333)	333	230	177	125	79	47	27	16	6	2	1	0
TPC (N = 166)	166	73	39	16	6	5	2	1	0	0	0	0

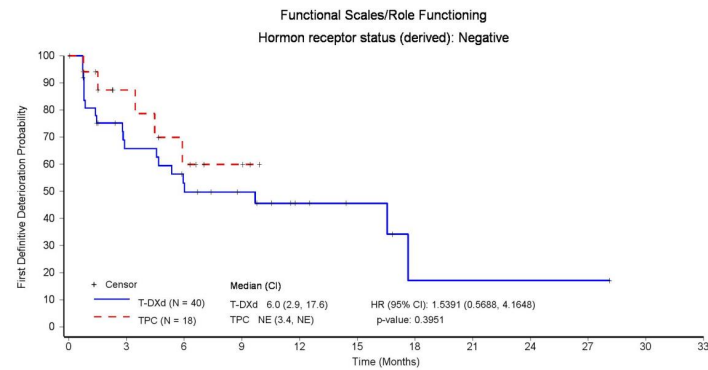
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:16; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_DD\_4\_FAS.rf



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Patients still at risk:

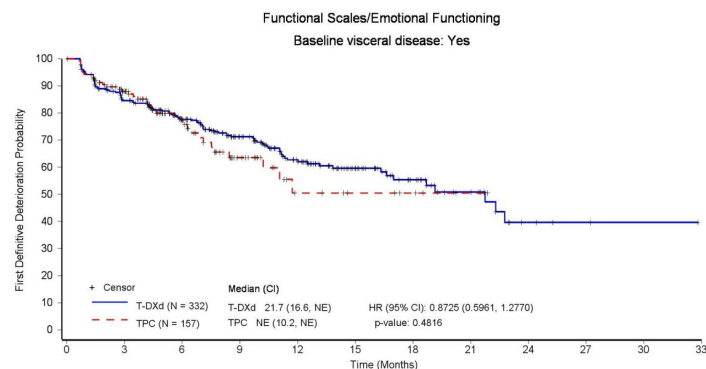
T-DXd (N = 40)	40	21	16	12	6	4	1	1	1	1	0	0
TPC (N = 18)	18	10	6	3	0	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 Final



Patients still at risk:

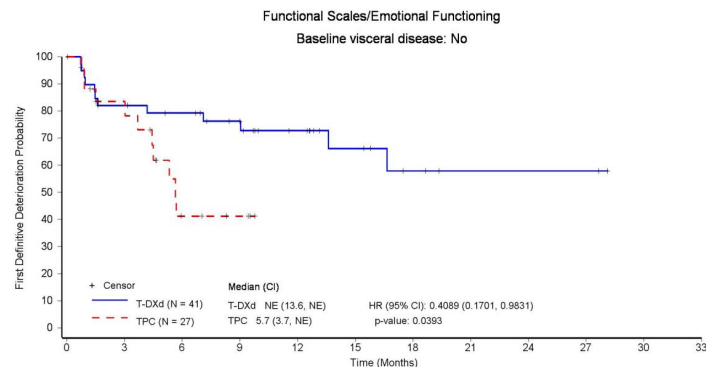
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 332)	332	249	198	145	93	57	33	18	4	2	1	0
TPC (N = 157)	157	99	56	24	9	6	4	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:16; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_DD\_4\_FAS.rtf

Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.3.6.4 - EORTC QLQ-C30 - Definitive deterioration - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

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Patients still at risk:

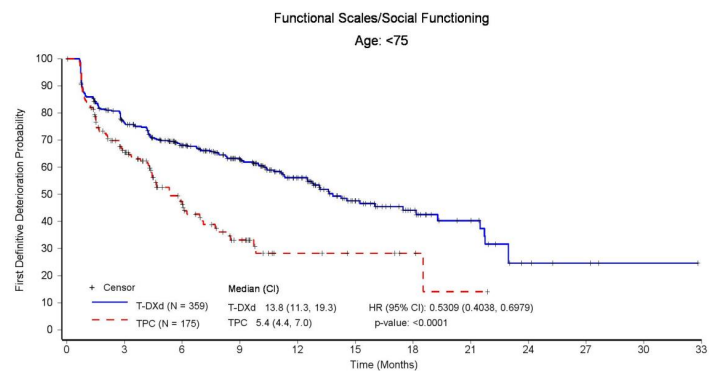
T-DXd (N = 41)	41	31	28	23	16	10	5	2	2	2	0	0
TPC (N = 27)	27	16	5	3	0	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:16; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_DD\_4\_FAS.rf

Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.3.6.4 - EORTC QLQ-C30 - Definitive deterioration - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

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Patients still at risk:

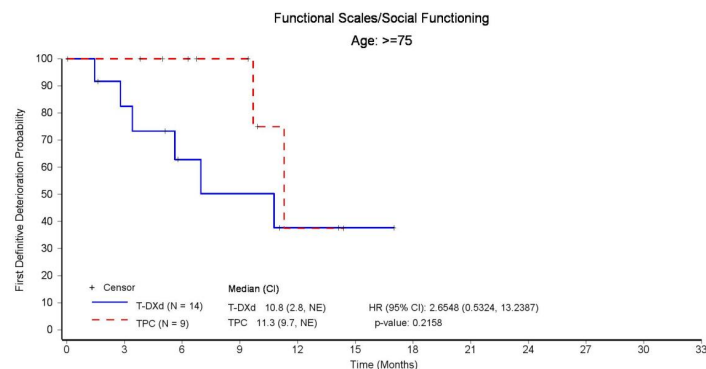
T-DXd (N = 359)	359	242	186	142	90	49	29	16	5	3	1	0
TPC (N = 175)	175	88	43	20	7	5	3	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:16; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_DD\_4\_FAS.rf

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 Data Intelligence – Evidence Generation  
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Patients still at risk:

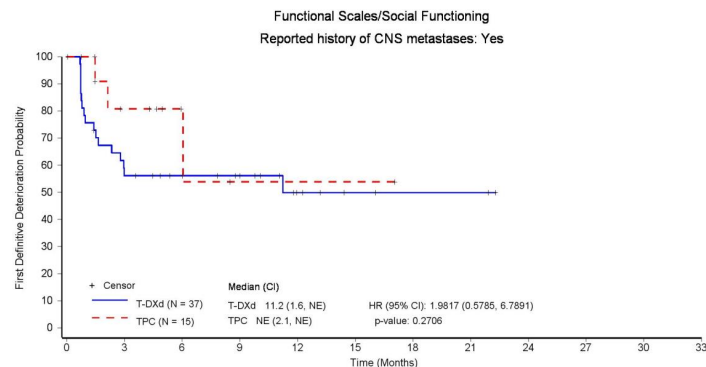
T-DXd (N = 14)	14	9	5	4	2	1	0	0	0	0	0
TPC (N = 9)	9	9	7	5	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:16; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_DD\_4\_FAS.rf

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 Data Intelligence – Evidence Generation  
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Patients still at risk:

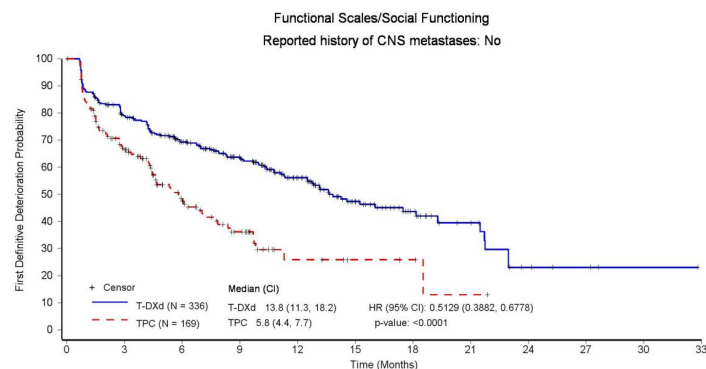
T-DXd (N = 37)	37	20	16	13	6	3	2	2	0	0	0	0
TPC (N = 15)	15	7	3	1	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:16; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_DD\_4\_FAS.rf

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Patients still at risk:

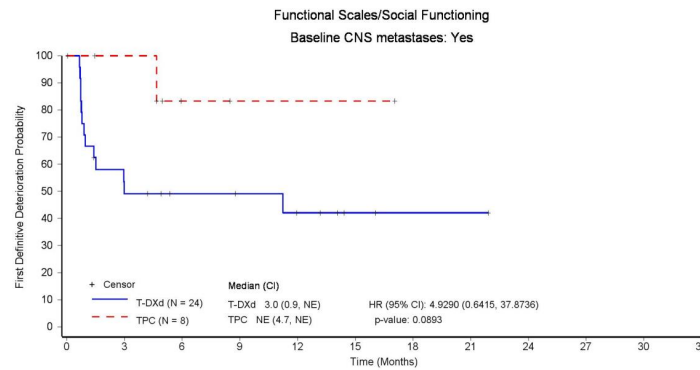
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 336)	336	231	175	133	86	47	27	14	5	3	1	0
TPC (N = 169)	169	90	47	24	7	4	3	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:16; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_DD\_4\_FAS.rf

Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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Patients still at risk:

T-DXd (N = 24)	24	11	8	7	5	2	1	1	0	0	0	0
TPC (N = 8)	8	6	2	1	1	1	0	0	0	0	0	0

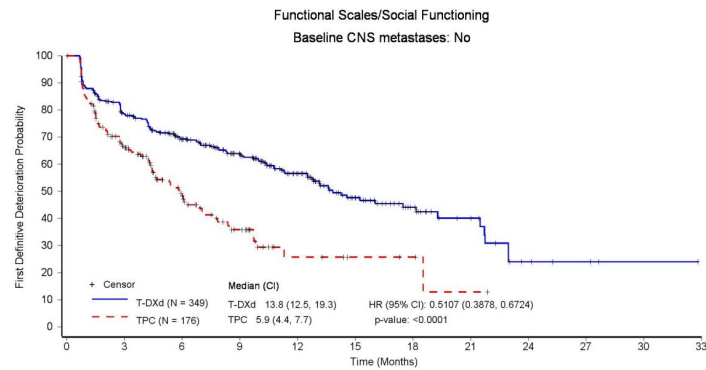
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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 Run date: 21OCT2022 – 18:16; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_DD\_4\_FAS.rf



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Patients still at risk:

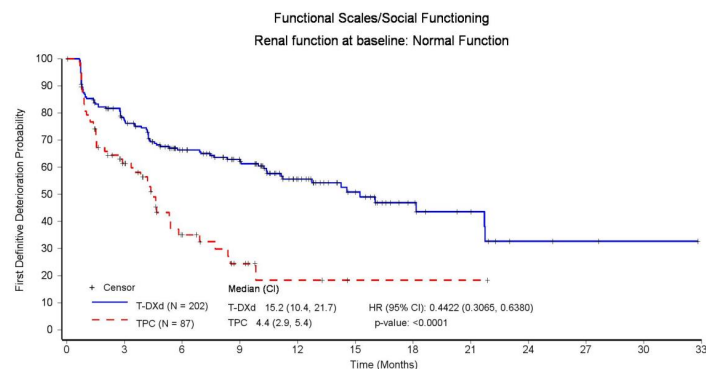
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 349)	349	240	183	139	87	48	28	15	5	3	1	0
TPC (N = 176)	176	91	48	24	7	4	3	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:16; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_DD\_4\_FAS.rf

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Patients still at risk:

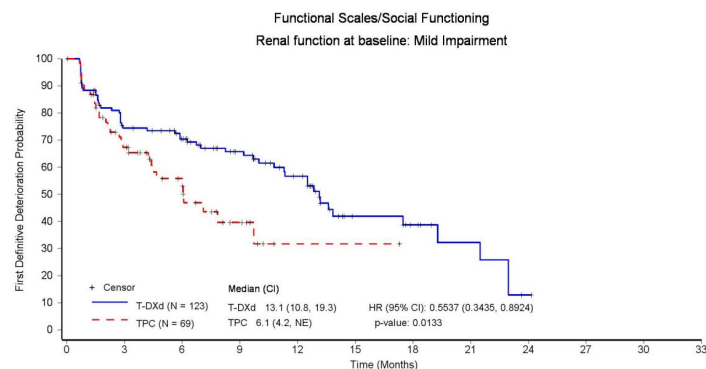
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 202)	202	140	102	80	46	29	15	9	3	2	1	0
TPC (N = 87)	87	39	16	7	3	1	1	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:16; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_DD\_4\_FAS.rf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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Patients still at risk:

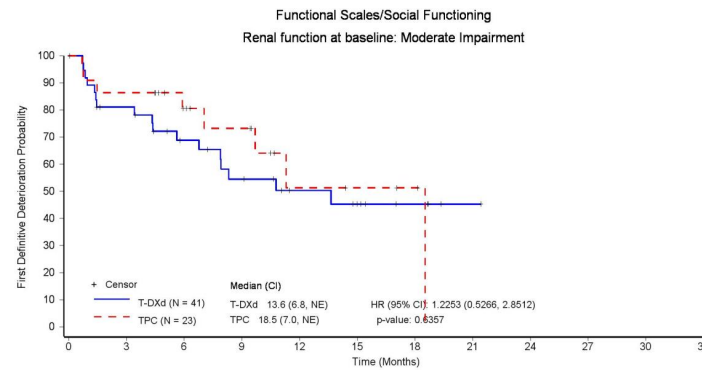
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 123)	123	79	67	49	34	13	9	5	1	0	0	0
TPC (N = 69)	69	36	20	8	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:16; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_DD\_4\_FAS.rf

Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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Patients still at risk:

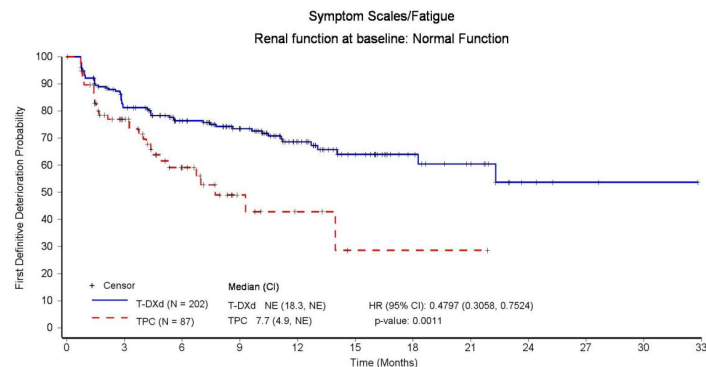
T-DXd (N = 41)	41	28	20	15	10	7	4	1	0	0	0	0
TPC (N = 23)	23	19	13	10	4	3	2	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:16; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_DD\_4\_FAS.rf

Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.3.6.4 - EORTC QLQ-C30 - Definitive deterioration - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

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Patients still at risk:

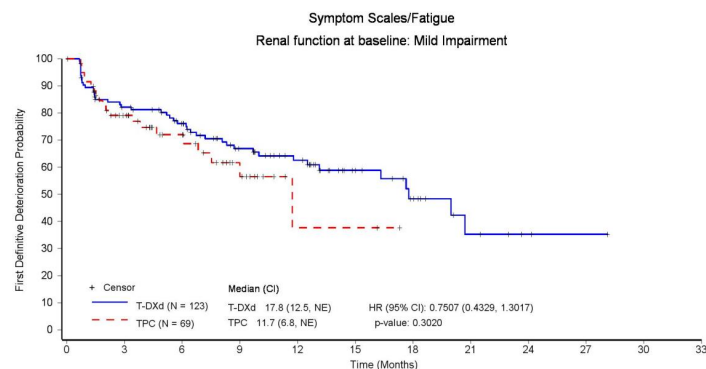
T-DXd (N = 202)	202	147	115	90	55	34	19	13	4	2	1	0
TPC (N = 87)	87	45	22	8	4	1	1	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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Patients still at risk:

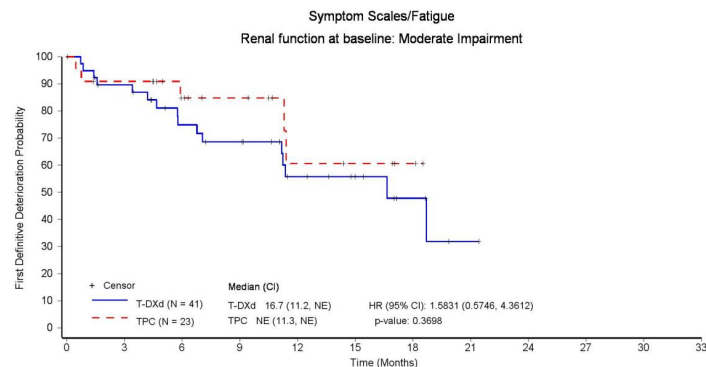
T-DXd (N = 123)	123	87	72	52	39	21	12	5	2	1	0	0
TPC (N = 69)	69	39	24	12	2	2	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
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Patients still at risk:

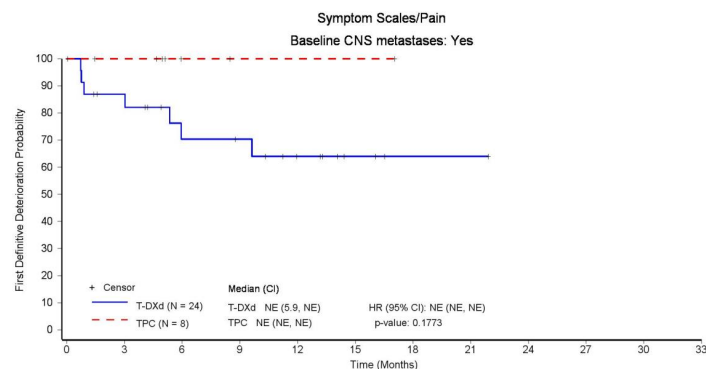
T-DXd (N = 41)	41	33	24	21	12	8	4	1	0	0	0	0
TPC (N = 23)	23	19	13	10	5	4	2	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 24)	24	18	12	11	7	3	1	1	0	0	0	0
TPC (N = 8)	8	6	2	1	1	1	0	0	0	0	0	0

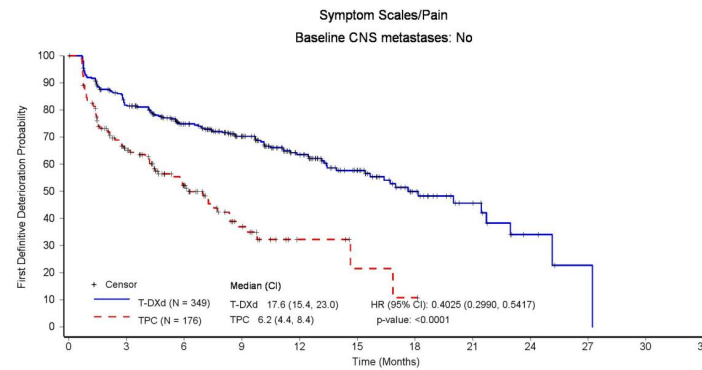
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Patients still at risk:

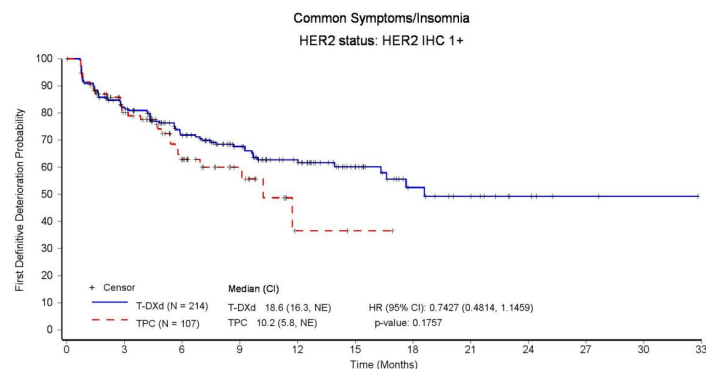
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 349)	349	253	196	148	92	56	31	15	4	1	0	0
TPC (N = 176)	176	85	47	19	5	2	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

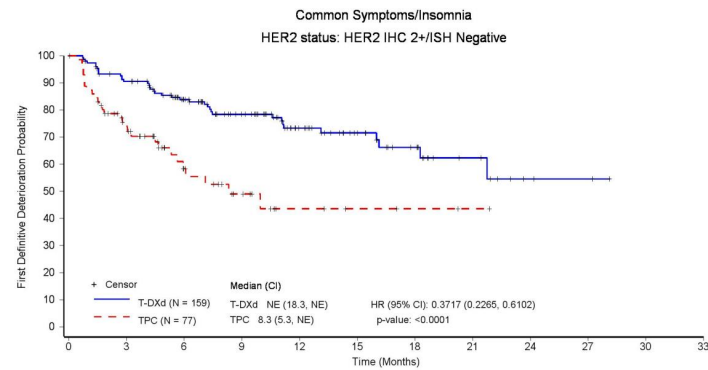
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 214)	214	151	112	85	60	33	16	11	5	2	1	0
TPC (N = 107)	107	58	31	14	2	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:16; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCC30\_DD\_4\_FAS.rtf

Daiichi Sankyo  
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 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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Patients still at risk:

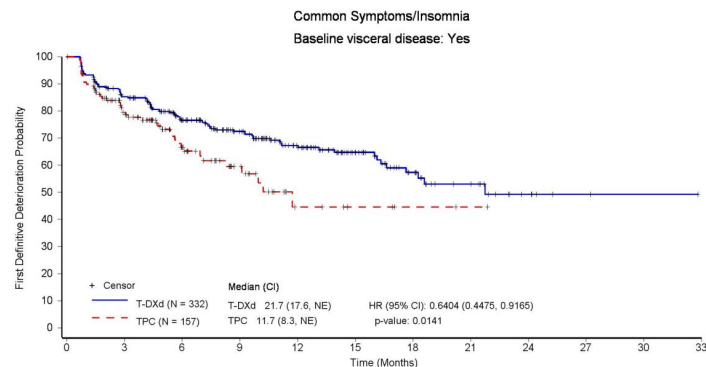
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 159)	159	131	101	76	46	31	20	9	3	2	0	0
TPC (N = 77)	77	45	21	12	5	3	2	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

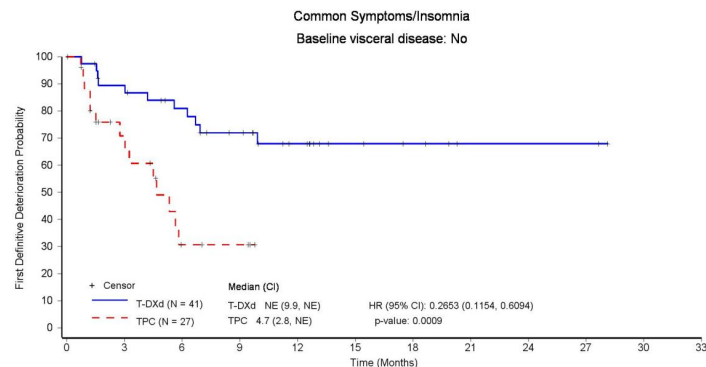
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 332)	332	249	186	140	92	56	31	18	6	2	1	0
TPC (N = 157)	157	89	48	23	7	4	2	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

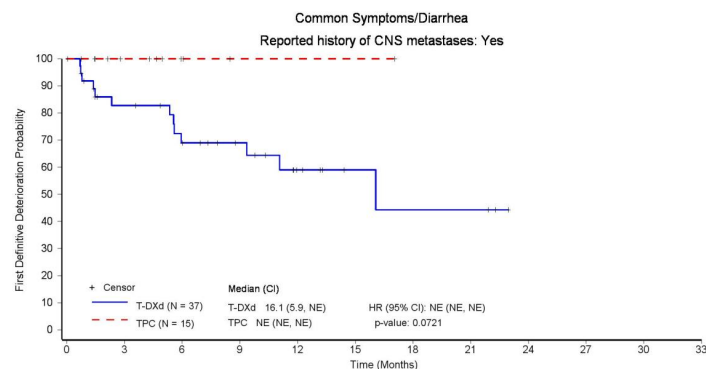
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 41)	41	33	27	21	14	8	5	2	2	2	0	0
TPC (N = 27)	27	14	4	3	0	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

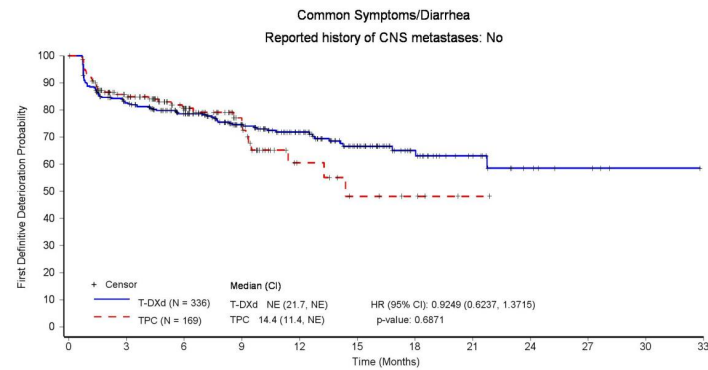
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 37)	37	26	20	15	8	4	3	3	0	0	0	0
TPC (N = 15)	15	8	3	1	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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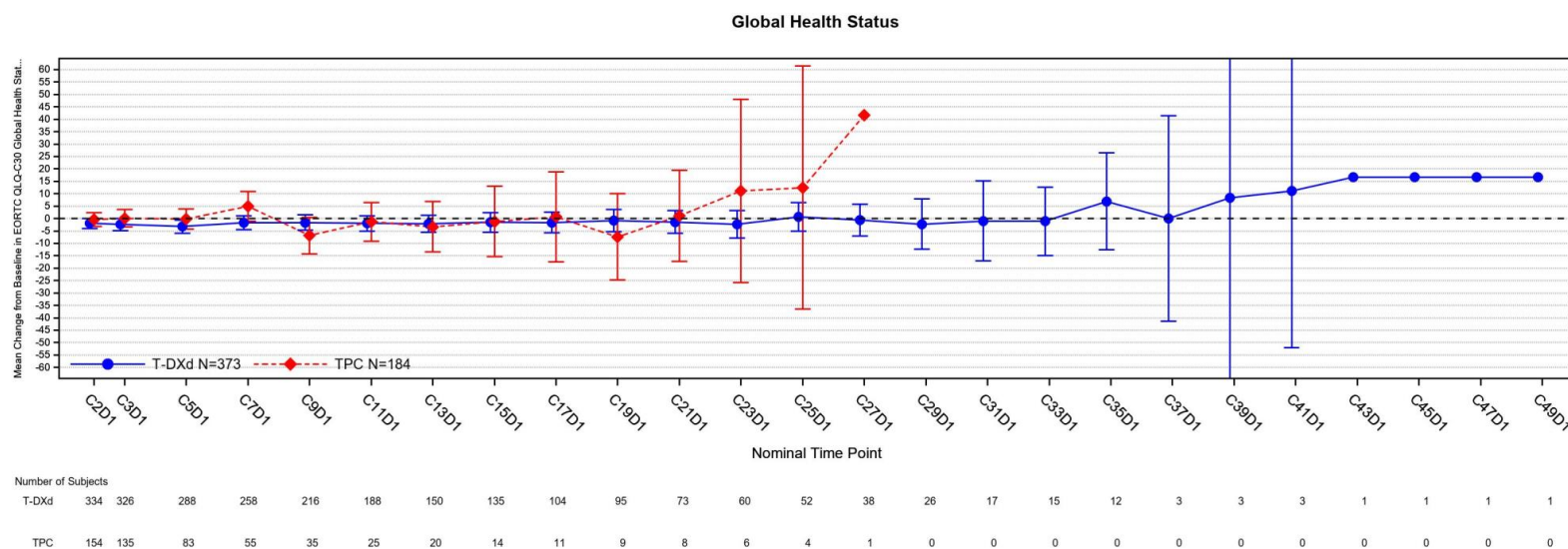
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.3.7.1 - EORTC QLQ-C30 - Mean change from baseline plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Number of subjects is number of subjects with an observation at the visit (i.e. scale score calculable for the visit). Error bars represent the 95% confidence interval for the mean value. A high score for EORTC-QLQ-C30 global health status represents a low/unhealthy level of functioning; a high score for a EORTC-QLQ-C30 and EORTC-QLQ-BR45 symptom scale/item represents a high level of symptomology/problems; a high score for a EORTC-QLQ-C30 and EORTC-QLQ-BR45 functional scale represents a low/unhealthy level of functioning A high score for the EQ-5D-5L VAS represents a low/unhealthy level of functioning;

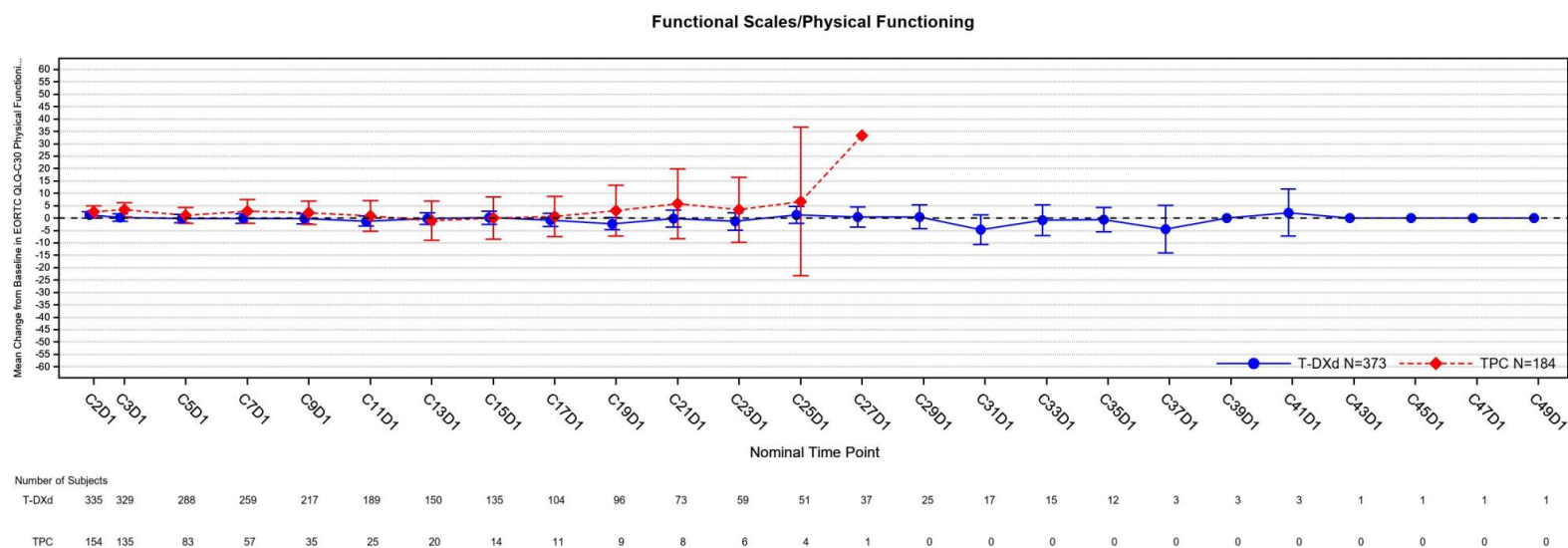
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DE.F.3.7.1 - EORTC QLQ-C30 - Mean change from baseline plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



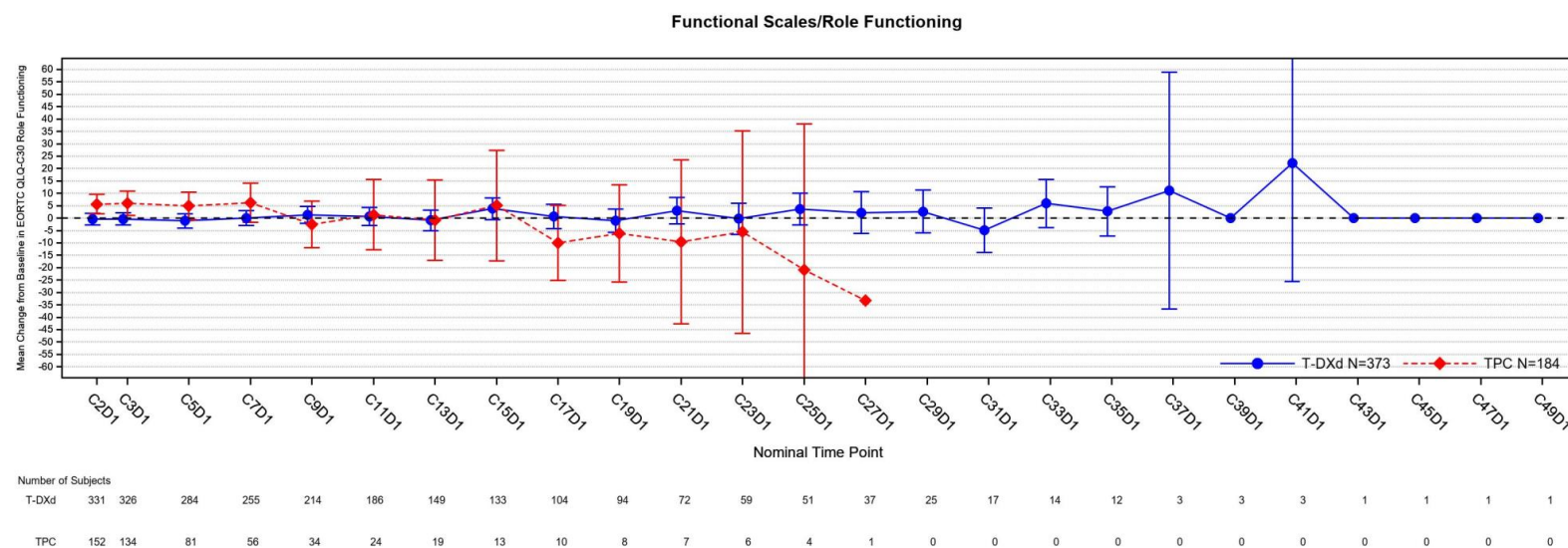
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DE.F.3.7.1 - EORTC QLQ-C30 - Mean change from baseline plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



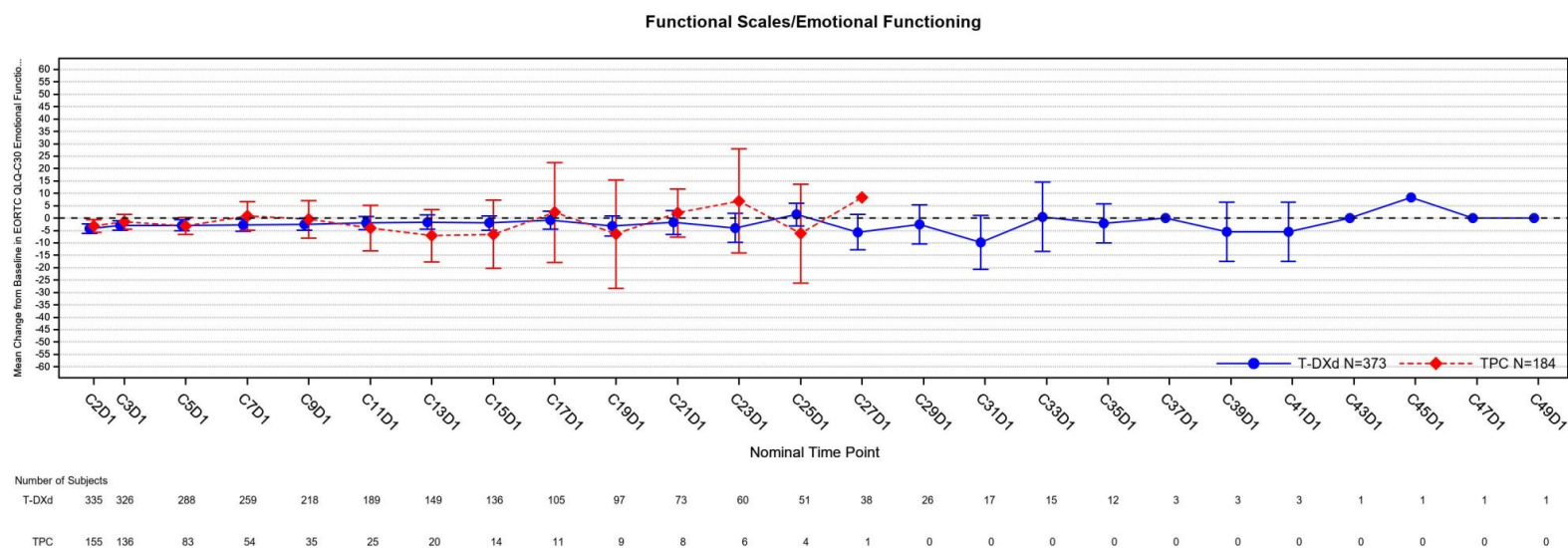
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DE.F.3.7.1 - EORTC QLQ-C30 - Mean change from baseline plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



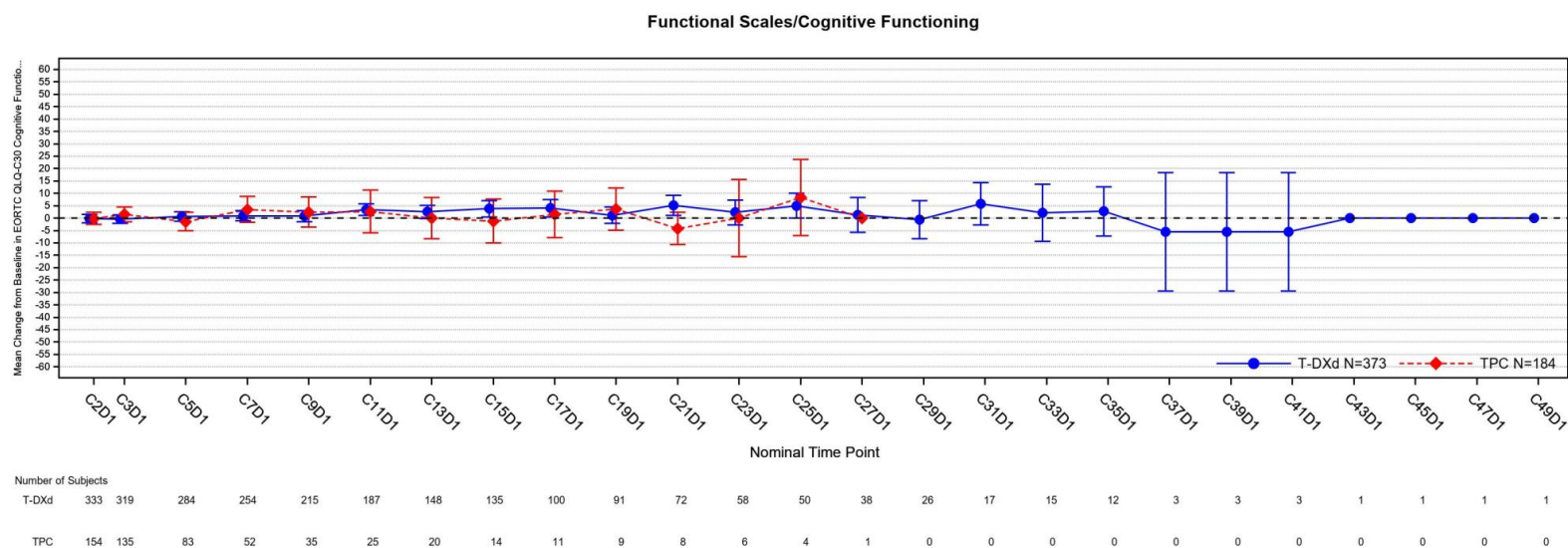
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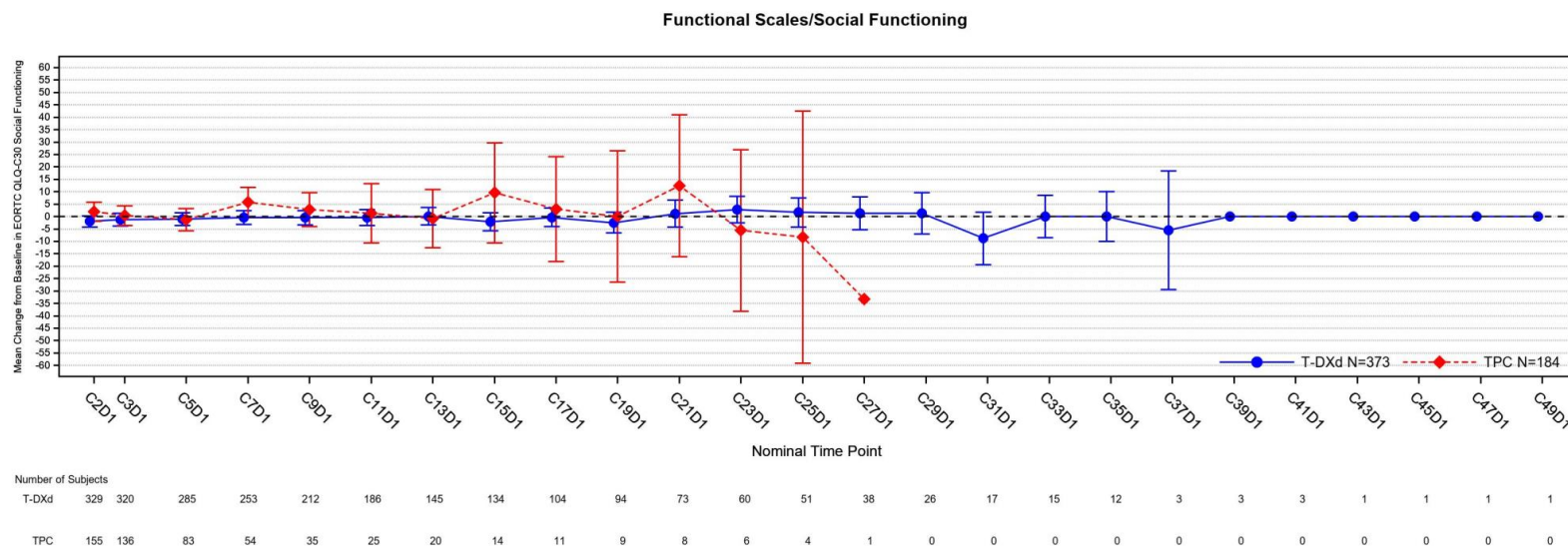
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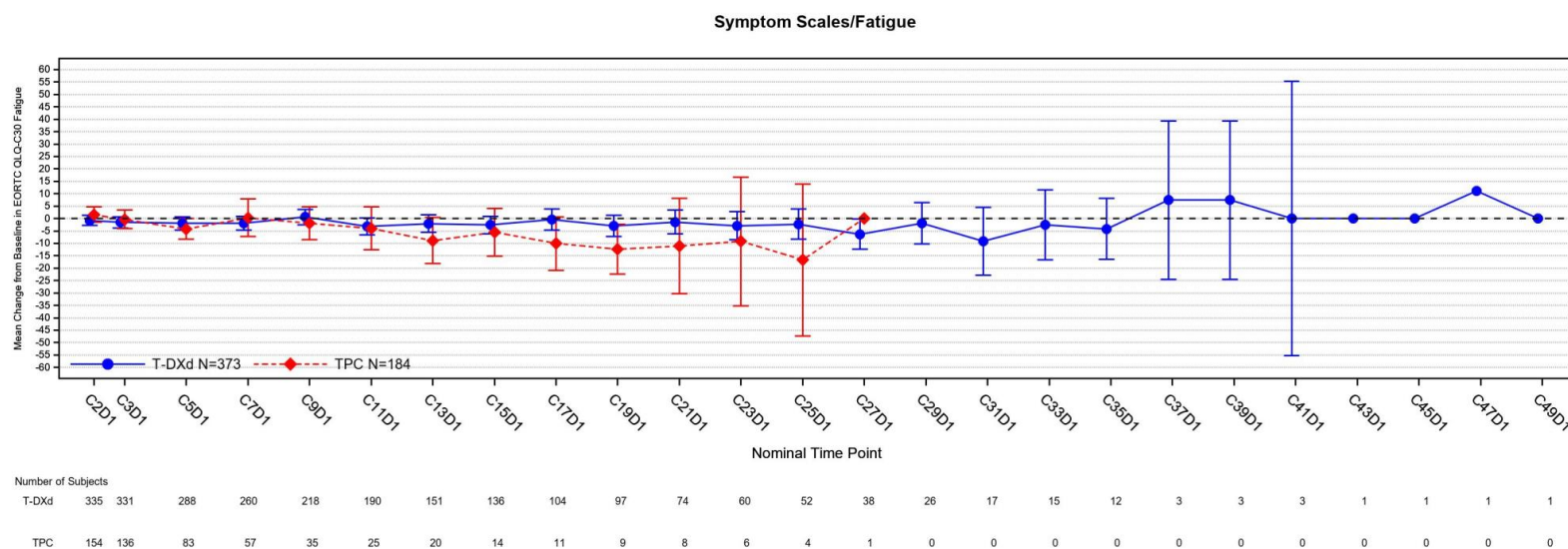
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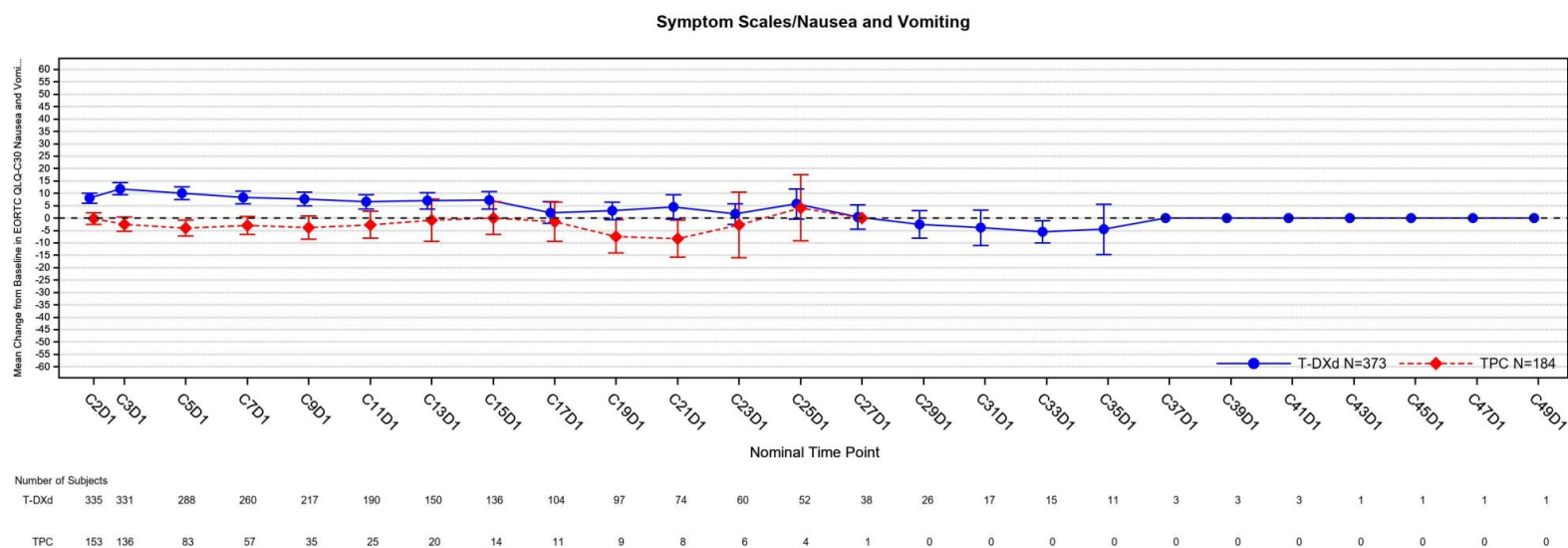
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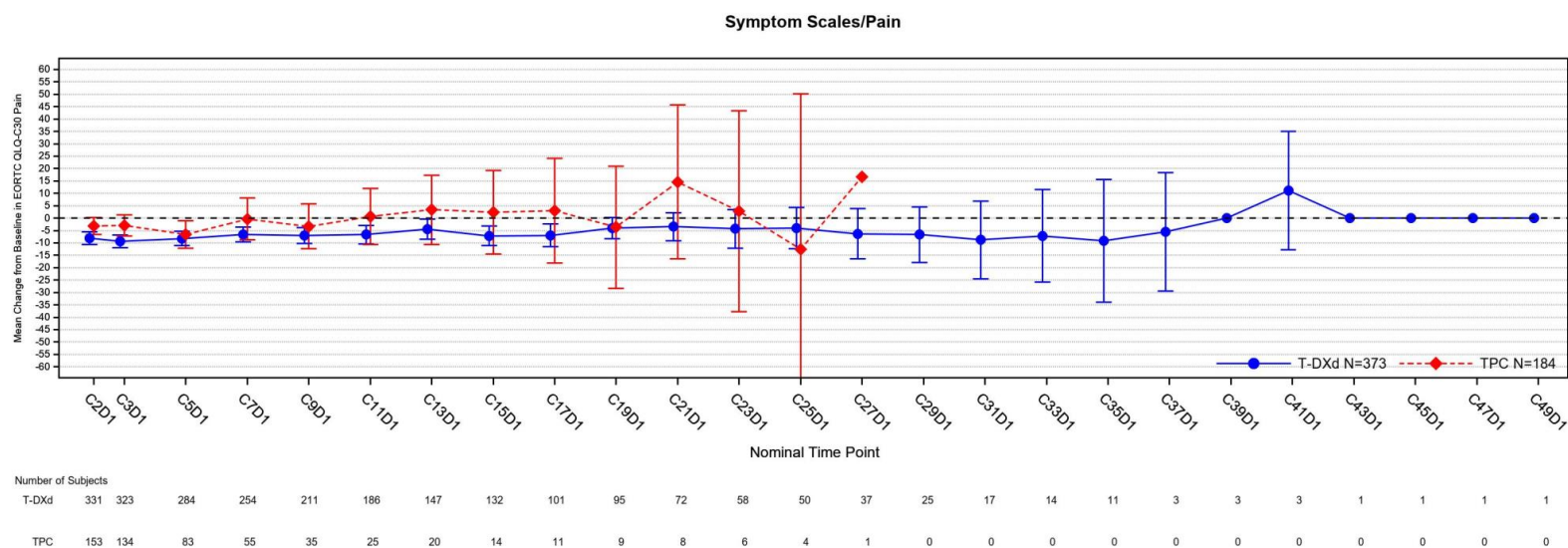
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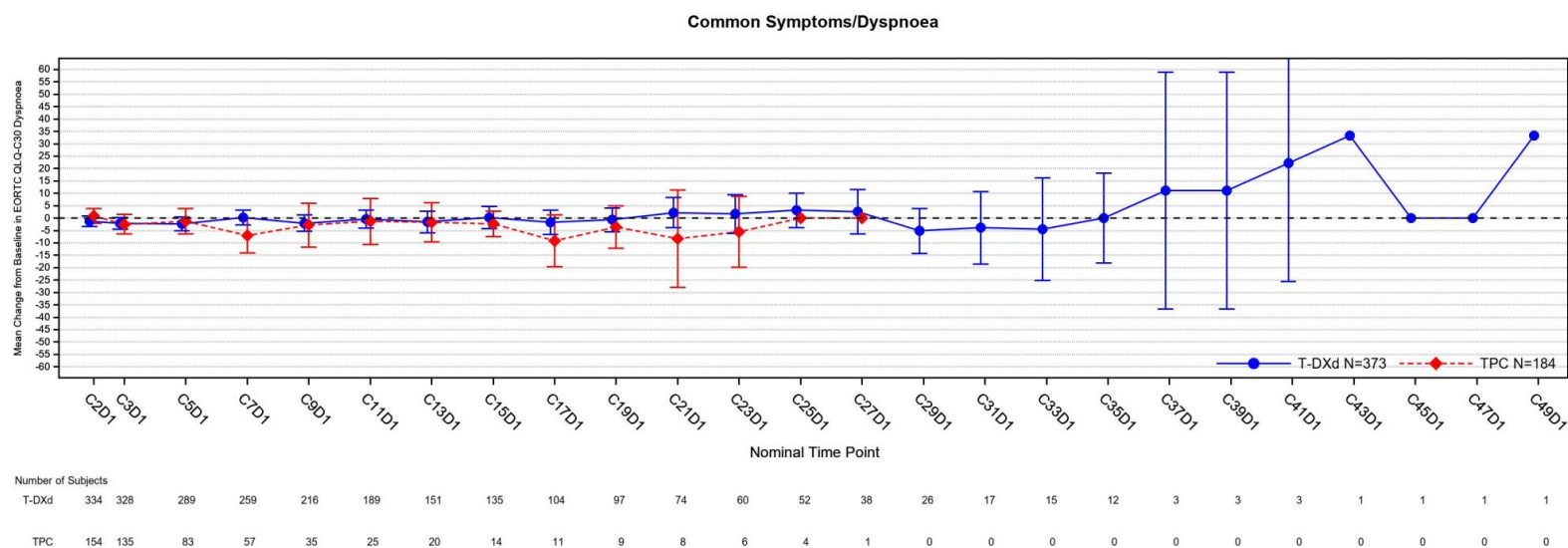
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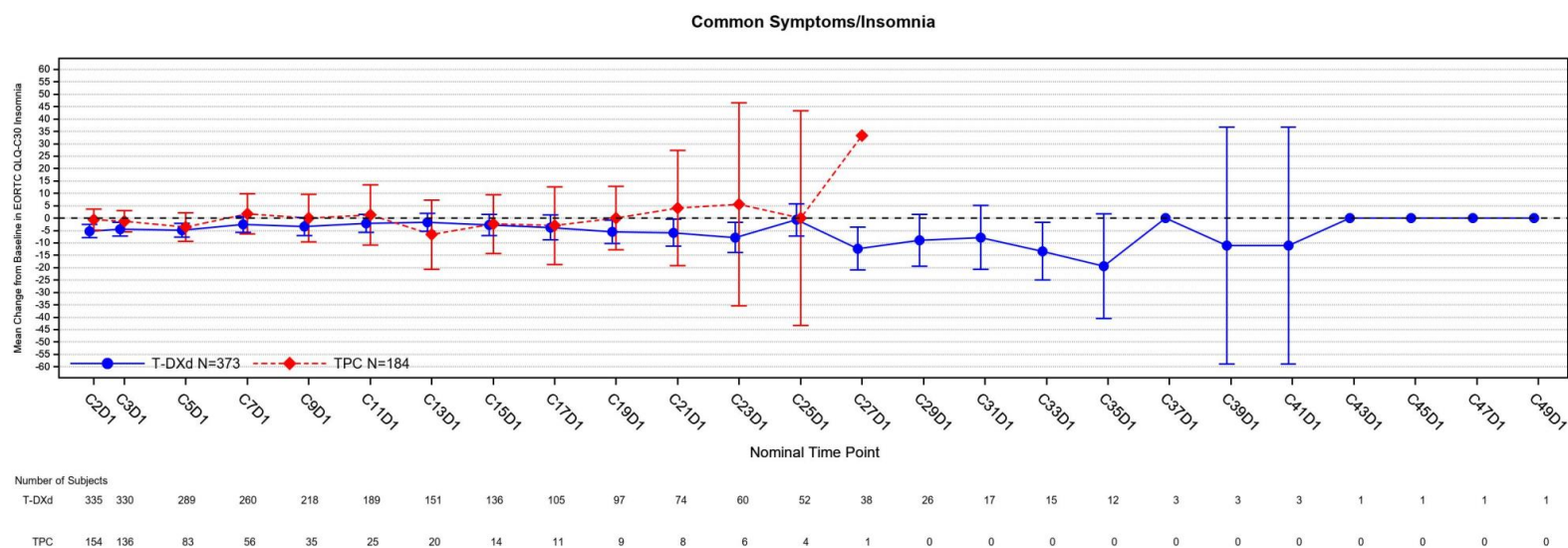
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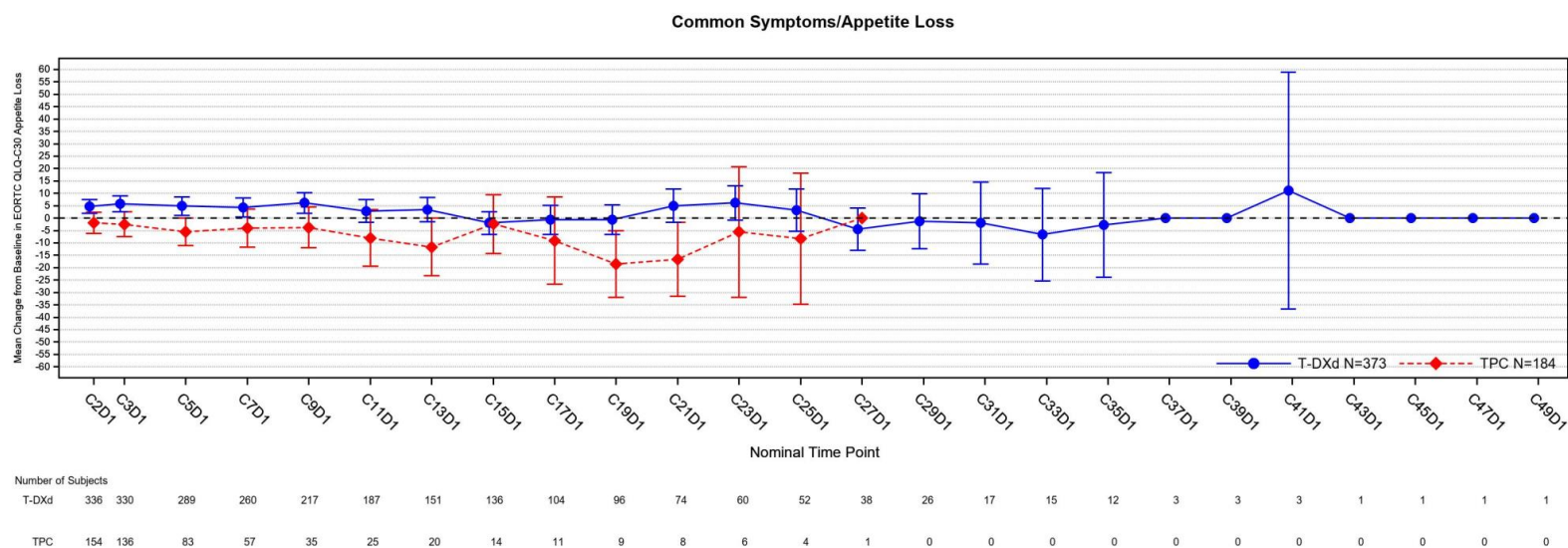
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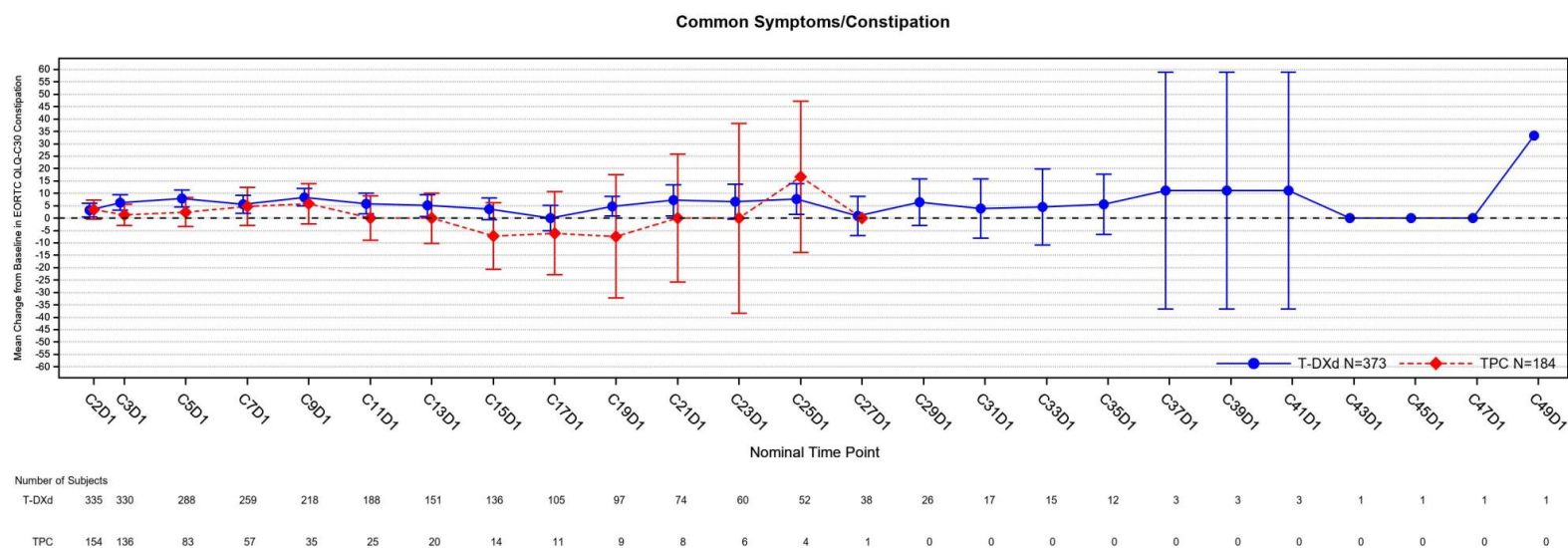
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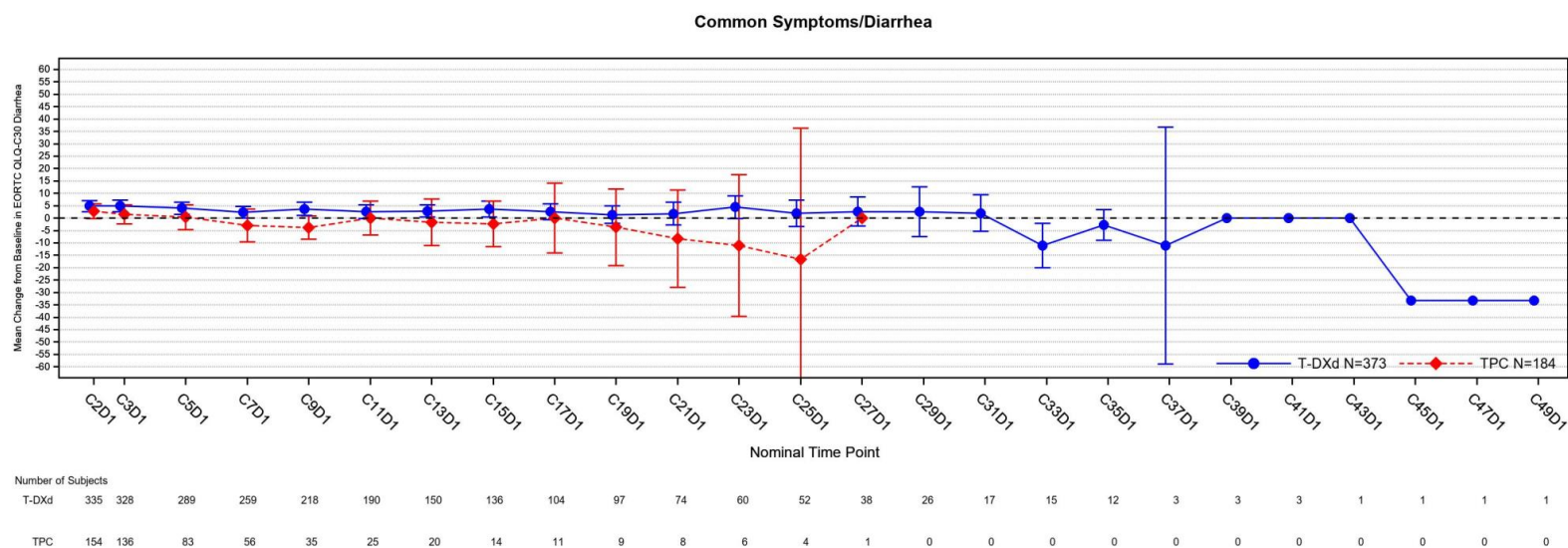
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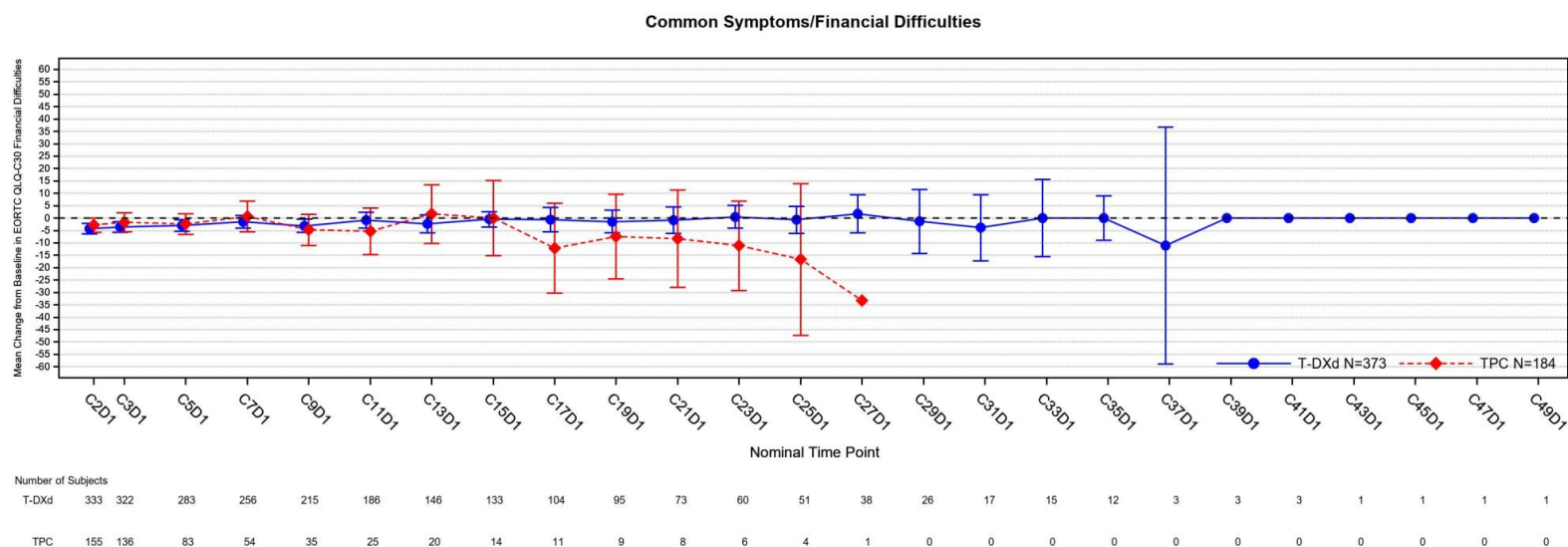
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Number of subjects is number of subjects with an observation at the visit (i.e. scale score calculable for the visit). Error bars represent the 95% confidence interval for the mean value. A high score for EORTC-QLQ-C30 global health status represents a low/unhealthy level of functioning; a high score for a EORTC-QLQ-C30 and EORTC-QLQ-BR45 symptom scale/item represents a high level of symptomology/problems; a high score for a EORTC-QLQ-C30 and EORTC-QLQ-BR45 functional scale represents a low/unhealthy level of functioning A high score for the EQ-5D-5L VAS represents a low/unhealthy level of functioning;

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Global Health Status\*

Parameter	n[a]	Estimate [b]	Standard Error	P-value
Intercept		-4.59	2.937	0.1187
Treatment				
T-DXd	350	-3.11	1.871	0.0972
TPC	164	0		
Time of Visit		0.02	0.005	<0.0001
Treatment*Time of Visit		-0.01	0.005	0.0482

A negative estimate denotes an improvement in health status in terms of the scale/item being evaluated.

[a] n is the number of subjects included in the model in each treatment group.

[b] Estimates obtained from a mixed model including terms for treatment, the randomization stratification factors, time of visit (days), and treatment-by-time of visit interaction as well as the intercept as random effect.

\* Unstructured covariance matrix was used to model the correlation within subject; † AR(1) covariance structure used to model correlation within subjects; ‡ Compound symmetry covariance structure used to model correlation within subjects

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Functional Scales/Physical Functioning\*

Parameter	n[a]	Estimate [b]	Standard Error	P-value
Intercept		2.41	2.124	0.2575
Treatment				
T-DXd	351	-2.07	1.358	0.1287
TPC	165	0		
Time of Visit		0.02	0.004	<0.0001
Treatment*Time of Visit		-0.02	0.004	<0.0001

A negative estimate denotes an improvement in health status in terms of the scale/item being evaluated.

[a] n is the number of subjects included in the model in each treatment group.

[b] Estimates obtained from a mixed model including terms for treatment, the randomization stratification factors, time of visit (days), and treatment-by-time of visit interaction as well as the intercept as random effect.

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Functional Scales/Role Functioning\*

Parameter	n[a]	Estimate [b]	Standard Error	P-value
Intercept		2.79	3.390	0.4103
Treatment				
T-DXd	351	-6.12	2.173	0.0050
TPC	163	0		
Time of Visit		0.02	0.006	0.0006
Treatment*Time of Visit		-0.01	0.006	0.0378

A negative estimate denotes an improvement in health status in terms of the scale/item being evaluated.

[a] n is the number of subjects included in the model in each treatment group.

[b] Estimates obtained from a mixed model including terms for treatment, the randomization stratification factors, time of visit (days), and treatment-by-time of visit interaction as well as the intercept as random effect.

\* Unstructured covariance matrix was used to model the correlation within subject; † AR(1) covariance structure used to model correlation within subjects; ‡ Compound symmetry covariance structure used to model correlation within subjects

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Functional Scales/Emotional Functioning\*

Parameter	n[a]	Estimate [b]	Standard Error	P-value
Intercept		-3.94	2.480	0.1126
Treatment				
T-DXd	351	-1.09	1.586	0.4904
TPC	165	0		
Time of Visit		0.02	0.004	<0.0001
Treatment*Time of Visit		-0.01	0.004	0.0041

A negative estimate denotes an improvement in health status in terms of the scale/item being evaluated.

[a] n is the number of subjects included in the model in each treatment group.

[b] Estimates obtained from a mixed model including terms for treatment, the randomization stratification factors, time of visit (days), and treatment-by-time of visit interaction as well as the intercept as random effect.

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Functional Scales/Cognitive Functioning\*

Parameter	n[a]	Estimate [b]	Standard Error	P-value
Intercept		0.23	2.231	0.9195
Treatment				
T-DXd	348	-0.88	1.433	0.5413
TPC	163	0		
Time of Visit		0.02	0.004	<0.0001
Treatment*Time of Visit		-0.01	0.004	0.0007

A negative estimate denotes an improvement in health status in terms of the scale/item being evaluated.

[a] n is the number of subjects included in the model in each treatment group.

[b] Estimates obtained from a mixed model including terms for treatment, the randomization stratification factors, time of visit (days), and treatment-by-time of visit interaction as well as the intercept as random effect.

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Functional Scales/Social Functioning\*

Parameter	n[a]	Estimate [b]	Standard Error	P-value
Intercept		1.70	3.074	0.5801
Treatment				
T-DXd	347	-3.11	1.970	0.1154
TPC	165	0		
Time of Visit		0.02	0.005	<0.0001
Treatment*Time of Visit		-0.01	0.006	0.0095

A negative estimate denotes an improvement in health status in terms of the scale/item being evaluated.

[a] n is the number of subjects included in the model in each treatment group.

[b] Estimates obtained from a mixed model including terms for treatment, the randomization stratification factors, time of visit (days), and treatment-by-time of visit interaction as well as the intercept as random effect.

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Symptom Scales/Fatigue\*

Parameter	n[a]	Estimate [b]	Standard Error	P-value
Intercept		-0.12	2.862	0.9667
Treatment				
T-DXd	352	-2.96	1.833	0.1065
TPC	164	0		
Time of Visit		0.01	0.005	0.1228
Treatment*Time of Visit		0.00	0.005	0.3410

A negative estimate denotes an improvement in health status in terms of the scale/item being evaluated.

[a] n is the number of subjects included in the model in each treatment group.

[b] Estimates obtained from a mixed model including terms for treatment, the randomization stratification factors, time of visit (days), and treatment-by-time of visit interaction as well as the intercept as random effect.

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Symptom Scales/Nausea and Vomiting\*

Parameter	n[a]	Estimate [b]	Standard Error	P-value
Intercept		-3.50	2.504	0.1630
Treatment				
T-DXd	352	10.78	1.623	<0.0001
TPC	165	0		
Time of Visit		0.00	0.005	0.4220
Treatment*Time of Visit		-0.02	0.005	0.0004

A negative estimate denotes an improvement in health status in terms of the scale/item being evaluated.

[a] n is the number of subjects included in the model in each treatment group.

[b] Estimates obtained from a mixed model including terms for treatment, the randomization stratification factors, time of visit (days), and treatment-by-time of visit interaction as well as the intercept as random effect.

\* Unstructured covariance matrix was used to model the correlation within subject; † AR(1) covariance structure used to model correlation within subjects; ‡ Compound symmetry covariance structure used to model correlation within subjects

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Symptom Scales/Pain\*

Parameter	n[a]	Estimate [b]	Standard Error	P-value
Intercept		-10.26	3.390	0.0026
Treatment				
T-DXd	348	-6.21	2.150	0.0040
TPC	163	0		
Time of Visit		0.02	0.005	<0.0001
Treatment*Time of Visit		-0.01	0.006	0.0246

A negative estimate denotes an improvement in health status in terms of the scale/item being evaluated.

[a] n is the number of subjects included in the model in each treatment group.

[b] Estimates obtained from a mixed model including terms for treatment, the randomization stratification factors, time of visit (days), and treatment-by-time of visit interaction as well as the intercept as random effect.

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Common Symptoms/Dyspnoea\*

Parameter	n[a]	Estimate [b]	Standard Error	P-value
Intercept		-1.47	3.100	0.6361
Treatment				
T-DXd	352	-1.87	1.987	0.3477
TPC	165	0		
Time of Visit		0.00	0.005	0.6962
Treatment*Time of Visit		0.00	0.006	0.4070

A negative estimate denotes an improvement in health status in terms of the scale/item being evaluated.

[a] n is the number of subjects included in the model in each treatment group.

[b] Estimates obtained from a mixed model including terms for treatment, the randomization stratification factors, time of visit (days), and treatment-by-time of visit interaction as well as the intercept as random effect.

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Common Symptoms/Insomnia\*

Parameter	n[a]	Estimate [b]	Standard Error	P-value
Intercept		-3.14	3.475	0.3665
Treatment				
T-DXd	352	-4.32	2.230	0.0533
TPC	165	0		
Time of Visit		0.00	0.006	0.4619
Treatment*Time of Visit		0.00	0.007	0.9737

A negative estimate denotes an improvement in health status in terms of the scale/item being evaluated.

[a] n is the number of subjects included in the model in each treatment group.

[b] Estimates obtained from a mixed model including terms for treatment, the randomization stratification factors, time of visit (days), and treatment-by-time of visit interaction as well as the intercept as random effect.

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Common Symptoms/Appetite Loss\*

Parameter	n[a]	Estimate [b]	Standard Error	P-value
Intercept		-3.44	3.810	0.3666
Treatment				
T-DXd	352	8.11	2.443	0.0010
TPC	165	0		
Time of Visit		0.01	0.007	0.0409
Treatment*Time of Visit		-0.02	0.007	0.0008

A negative estimate denotes an improvement in health status in terms of the scale/item being evaluated.

[a] n is the number of subjects included in the model in each treatment group.

[b] Estimates obtained from a mixed model including terms for treatment, the randomization stratification factors, time of visit (days), and treatment-by-time of visit interaction as well as the intercept as random effect.

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Common Symptoms/Constipation\*

Parameter	n[a]	Estimate [b]	Standard Error	P-value
Intercept		0.98	3.482	0.7793
Treatment				
T-DXd	352	1.87	2.243	0.4042
TPC	165	0		
Time of Visit		0.01	0.007	0.3009
Treatment*Time of Visit		-0.01	0.007	0.1943

A negative estimate denotes an improvement in health status in terms of the scale/item being evaluated.

[a] n is the number of subjects included in the model in each treatment group.

[b] Estimates obtained from a mixed model including terms for treatment, the randomization stratification factors, time of visit (days), and treatment-by-time of visit interaction as well as the intercept as random effect.

\* Unstructured covariance matrix was used to model the correlation within subject; † AR(1) covariance structure used to model correlation within subjects; ‡ Compound symmetry covariance structure used to model correlation within subjects

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Common Symptoms/Diarrhea\*

Parameter	n[a]	Estimate [b]	Standard Error	P-value
Intercept		2.63	2.617	0.3161
Treatment				
T-DXd	351	2.29	1.696	0.1775
TPC	165	0		
Time of Visit		-0.01	0.005	0.0881
Treatment*Time of Visit		0.00	0.005	0.7726

A negative estimate denotes an improvement in health status in terms of the scale/item being evaluated.

[a] n is the number of subjects included in the model in each treatment group.

[b] Estimates obtained from a mixed model including terms for treatment, the randomization stratification factors, time of visit (days), and treatment-by-time of visit interaction as well as the intercept as random effect.

\* Unstructured covariance matrix was used to model the correlation within subject; † AR(1) covariance structure used to model correlation within subjects; ‡ Compound symmetry covariance structure used to model correlation within subjects

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Common Symptoms/Financial Difficulties\*

Parameter	n[a]	Estimate [b]	Standard Error	P-value
Intercept		0.00	2.812	0.9998
Treatment				
T-DXd	348	-1.46	1.804	0.4181
TPC	165	0		
Time of Visit		0.01	0.005	0.0189
Treatment*Time of Visit		-0.01	0.005	0.2040

A negative estimate denotes an improvement in health status in terms of the scale/item being evaluated.

[a] n is the number of subjects included in the model in each treatment group.

[b] Estimates obtained from a mixed model including terms for treatment, the randomization stratification factors, time of visit (days), and treatment-by-time of visit interaction as well as the intercept as random effect.

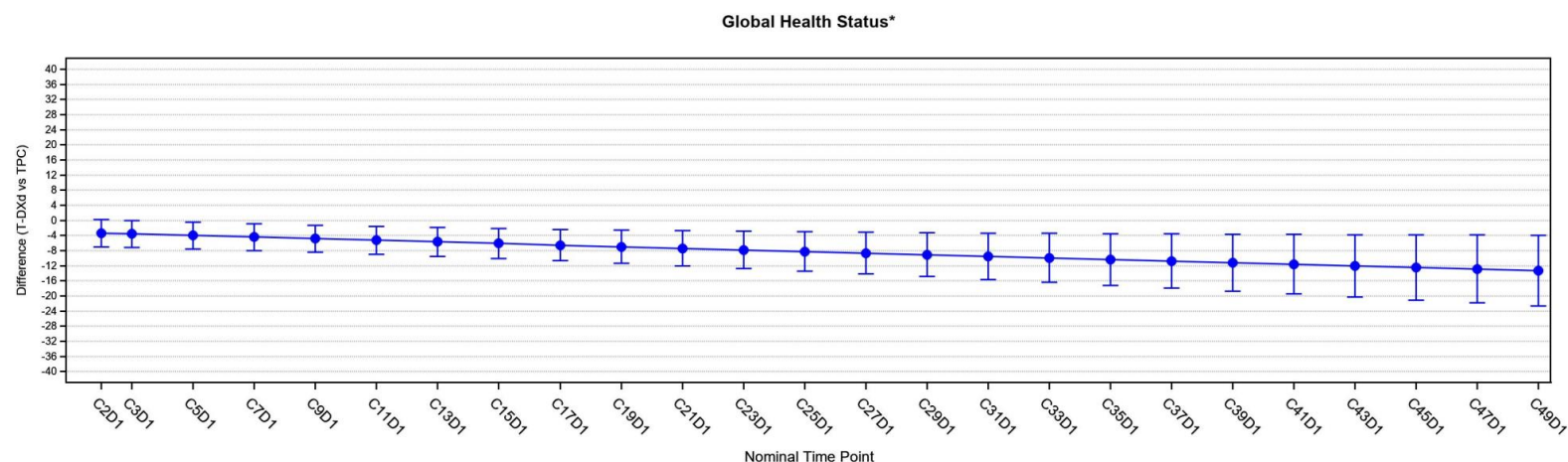
\* Unstructured covariance matrix was used to model the correlation within subject; † AR(1) covariance structure used to model correlation within subjects; ‡ Compound symmetry covariance structure used to model correlation within subjects

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Least square mean (LSM) estimates of trastuzumab deruxtecan versus comparator and their 95% CI are calculated using a restricted maximum likelihood (REML) based mixed model including terms for treatment, the randomization stratification factors, time of visit (days), and treatment by time of visit interaction as well as the intercept as random effect. A high score for global health status represents a low quality of life (change of direction from raw score); a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomology/problems.

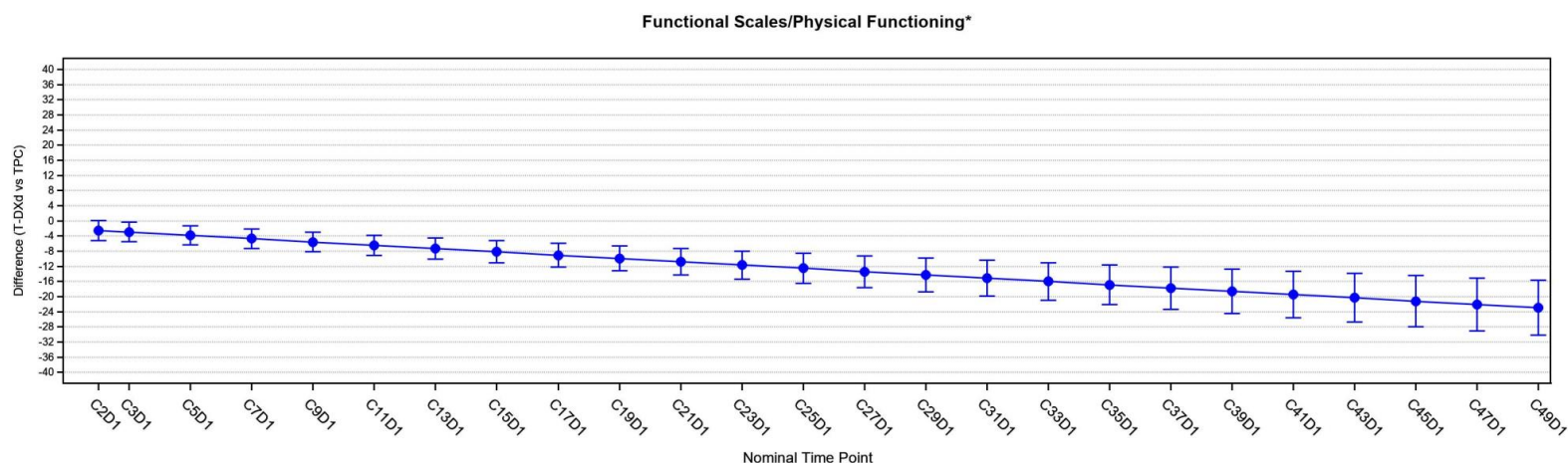
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Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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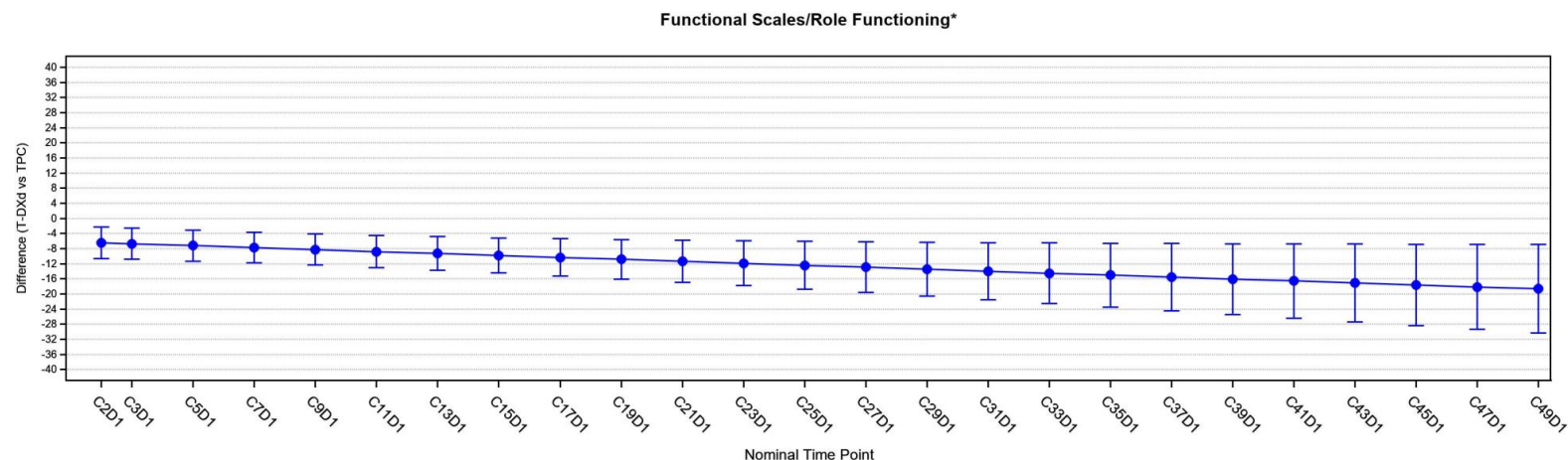
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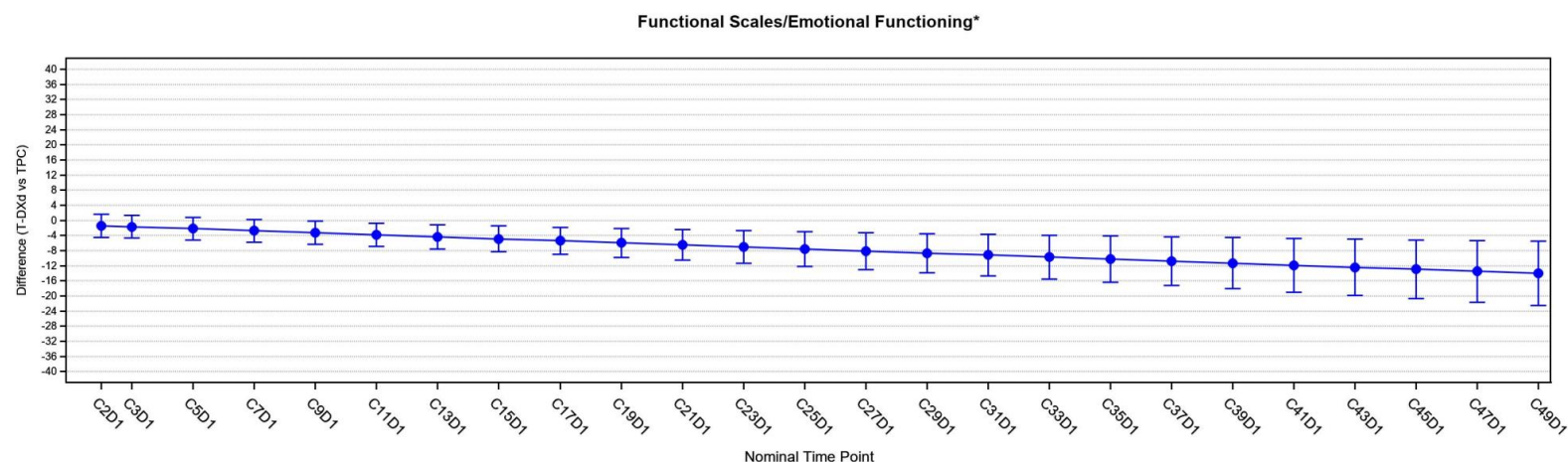
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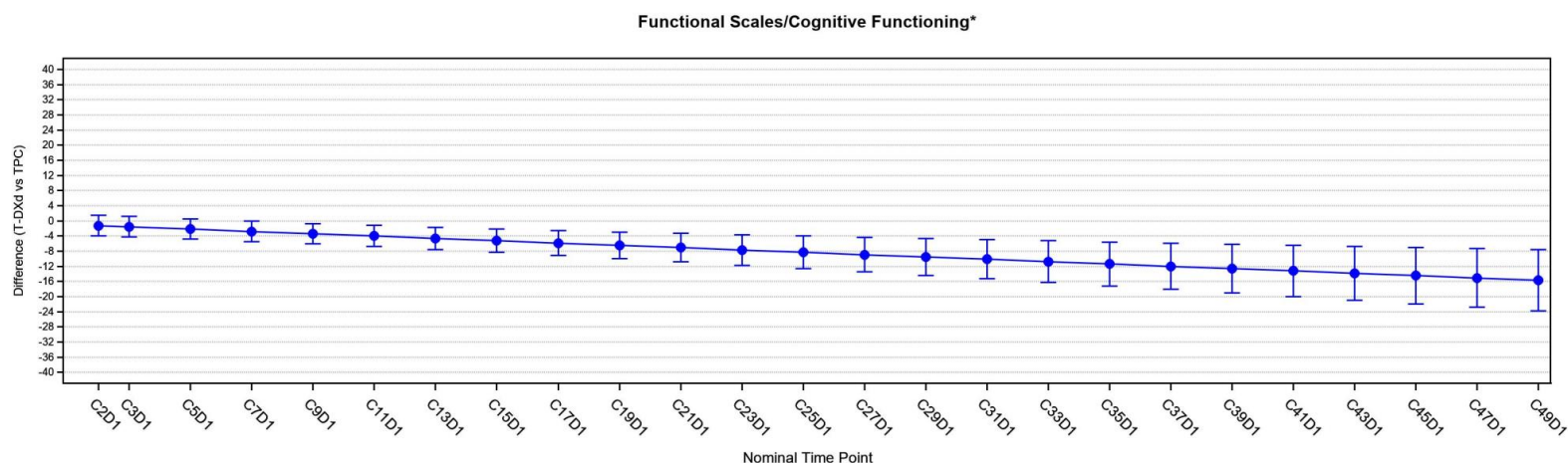
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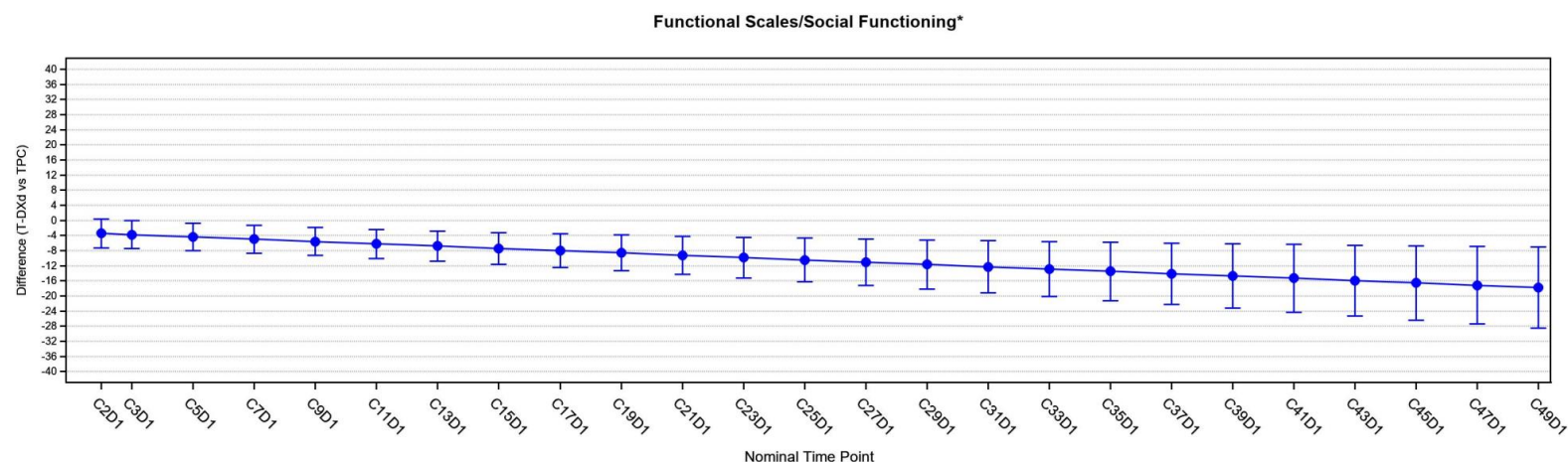
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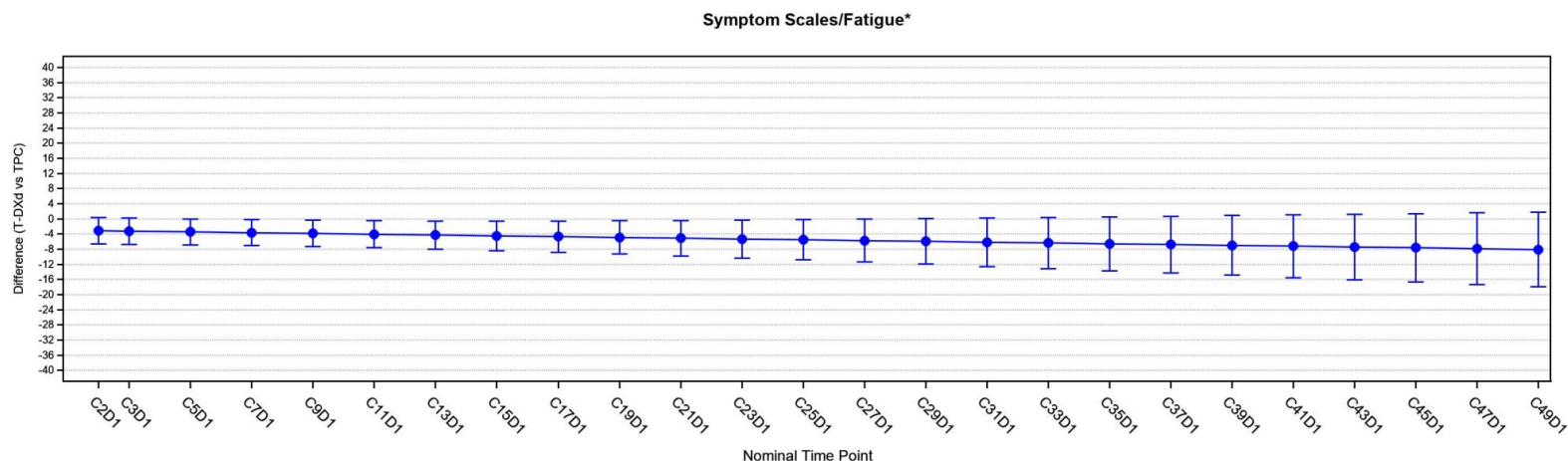
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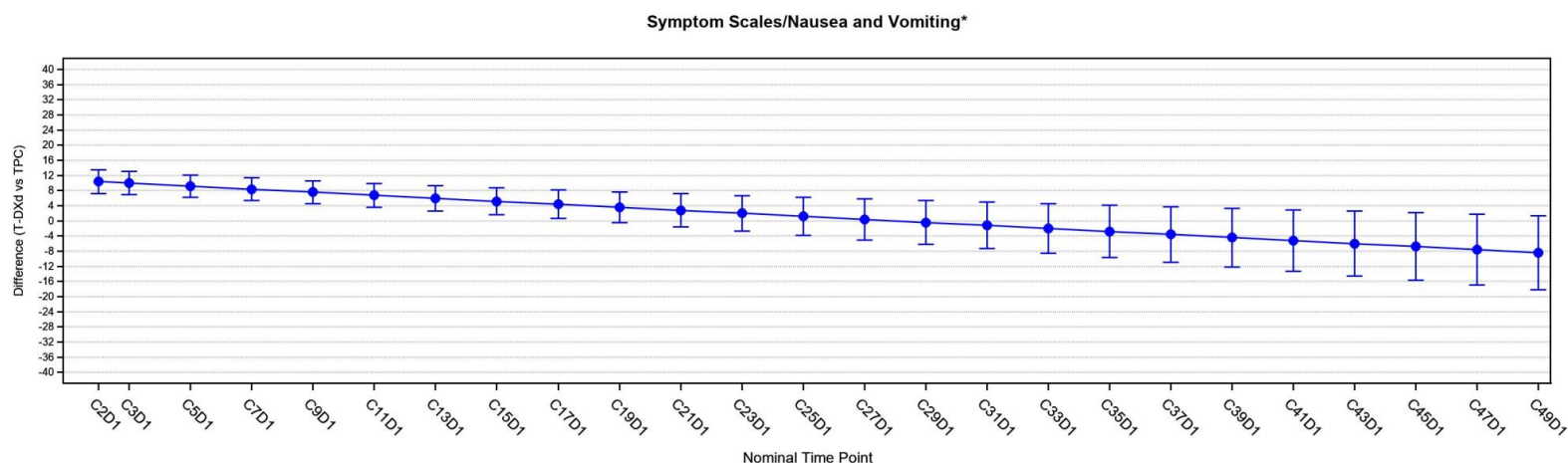
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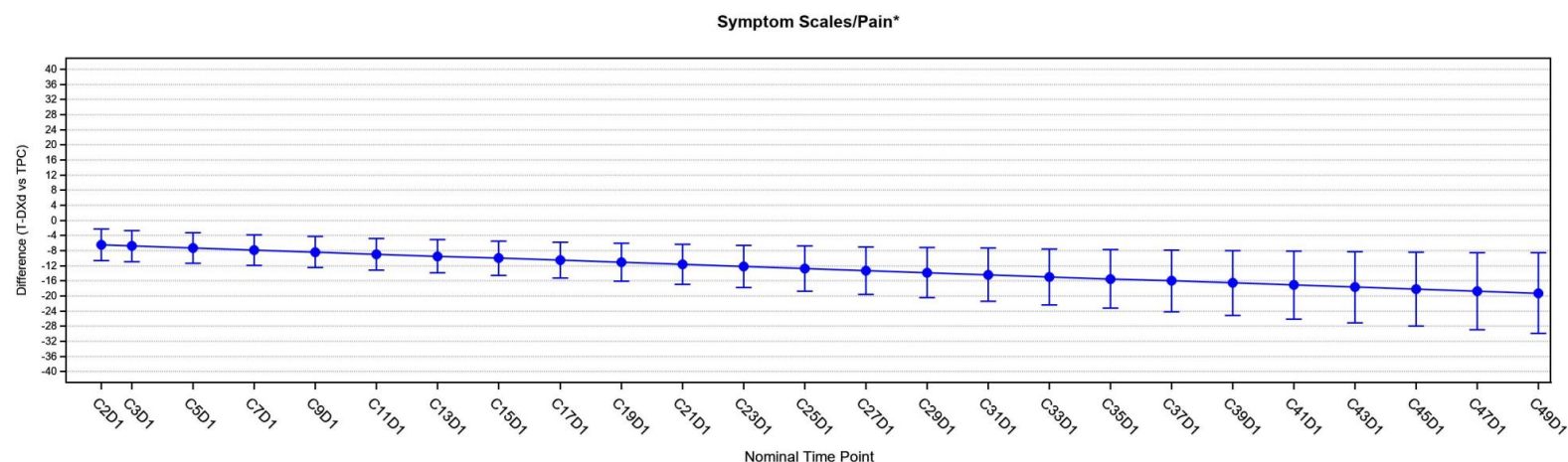
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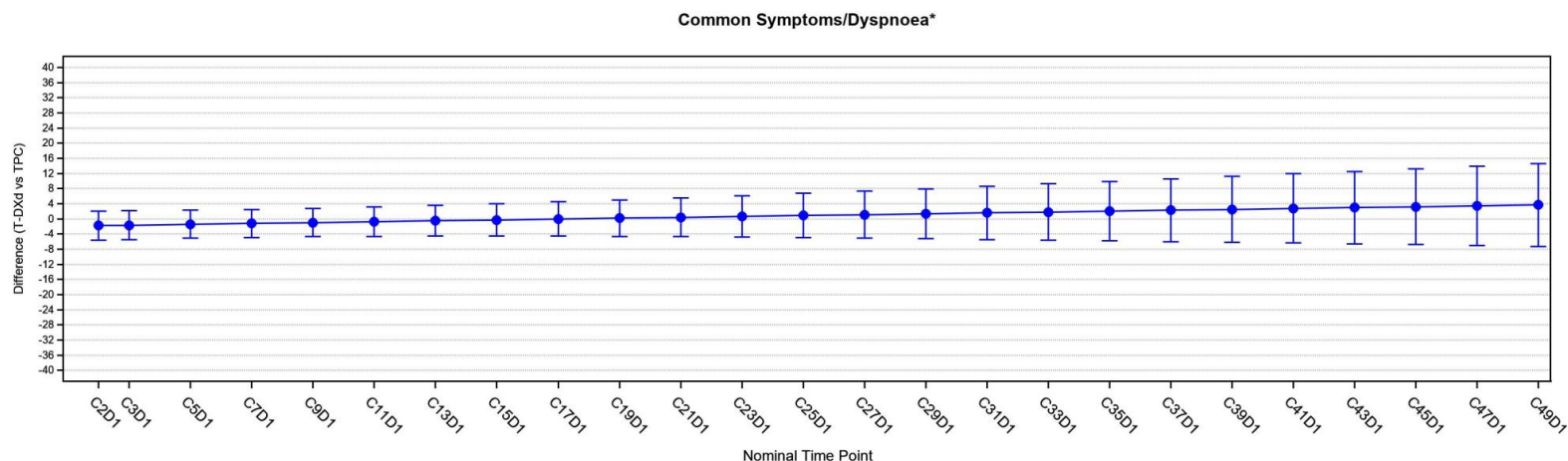
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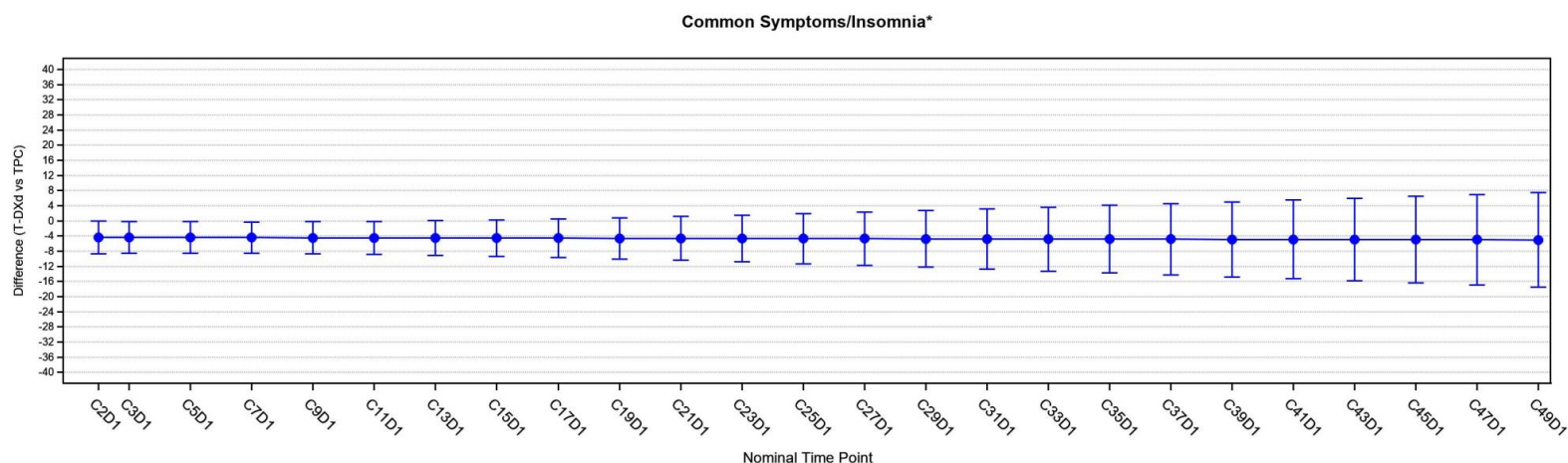
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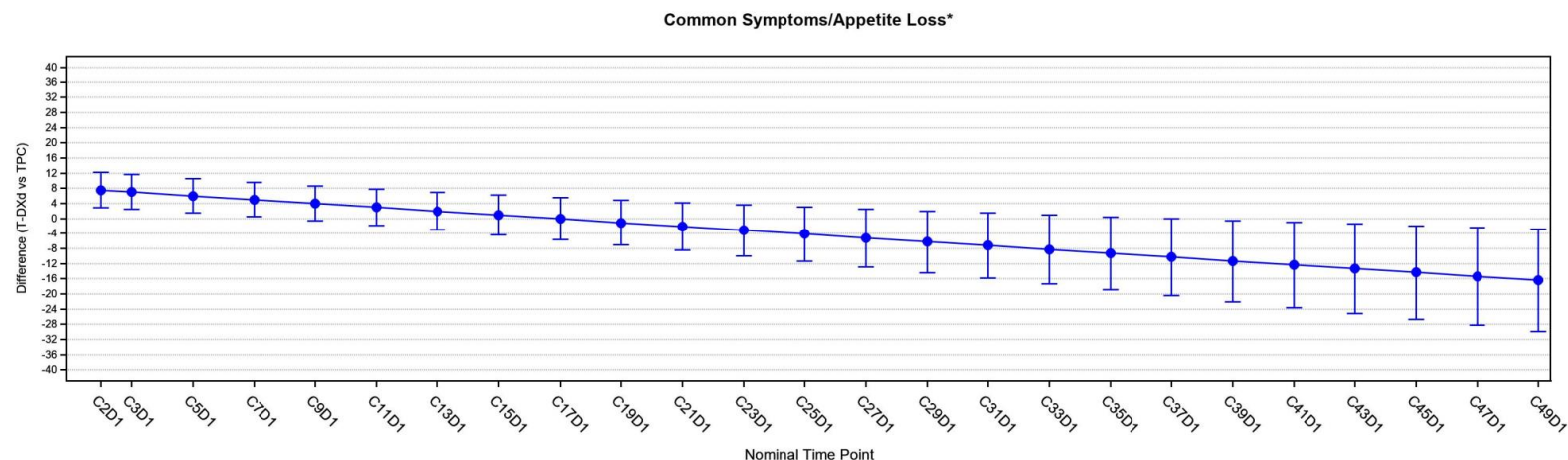
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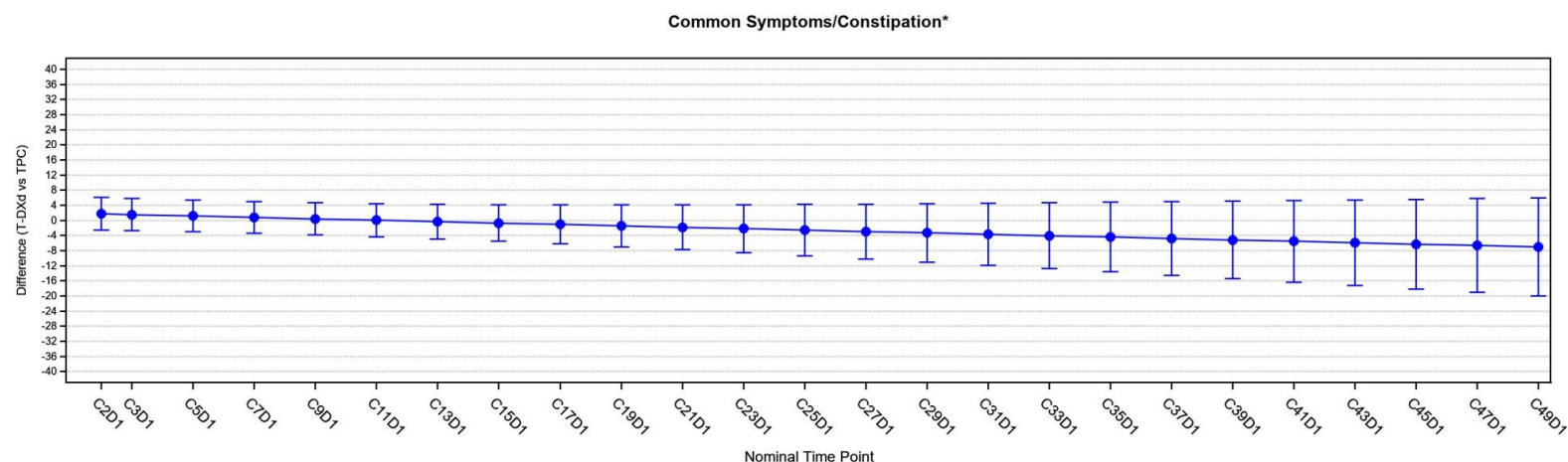
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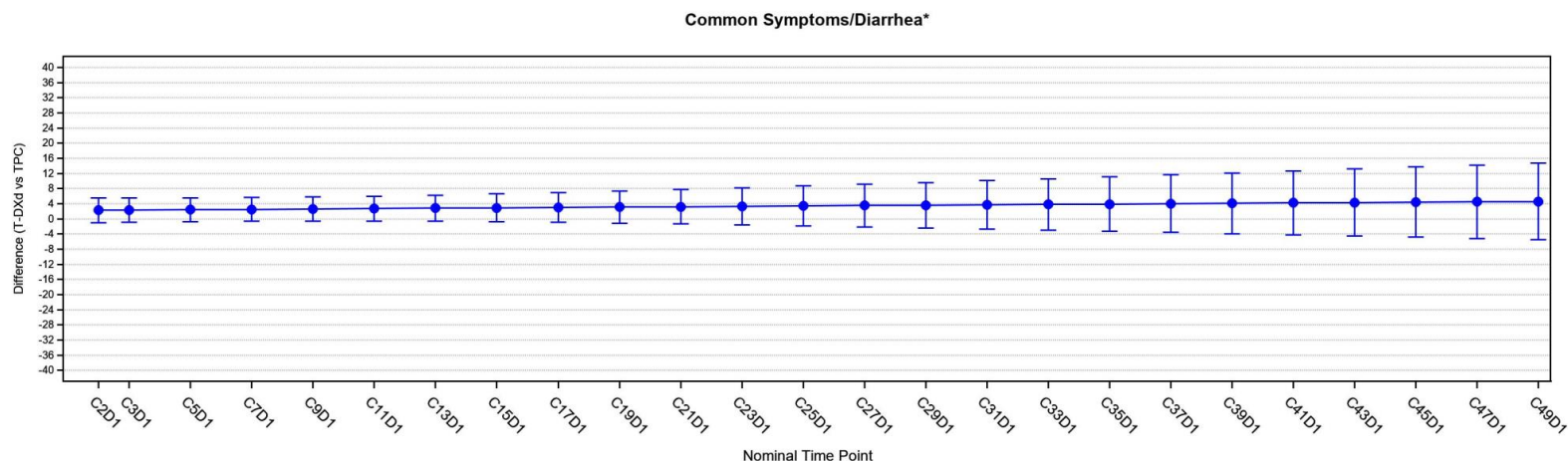
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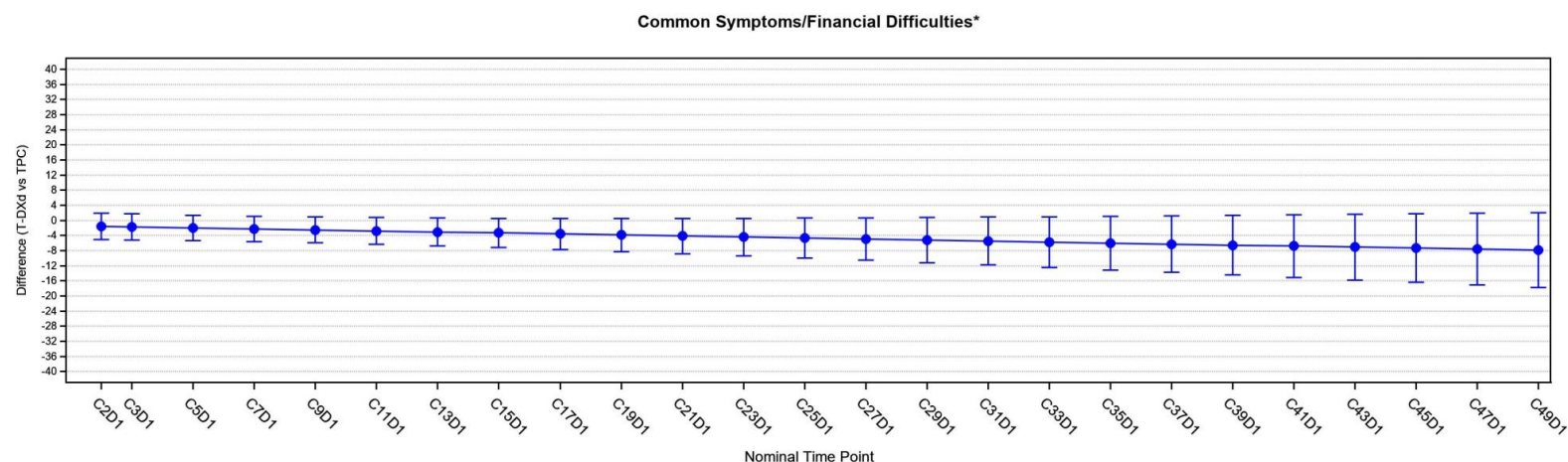
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**Anhang 4-G 3.3: EORTC QLQ-C30 (MID 10 Punkte)**

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DE.T.7.1.1 - EORTC QLQ-C30 - First deterioration 10 Points - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - Full Analysis Set

Global Health Status

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	210 (56.3)	99 (53.8)	
Number of subjects censored, n (%)	163 (43.7)	85 (46.2)	
Median time to first event (months) [a]	5.1	4.2	
95% Confidence Interval	[4.2, 7.0]	[2.8, 5.9]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.8224
95% Confidence Interval			[0.6449, 1.0488]
p-value			0.1150
Stratified log-rank p-value [c]			0.1103

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Functional Scales/Physical Functioning

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	187 (50.1)	99 (53.8)	
Number of subjects censored, n (%)	186 (49.9)	85 (46.2)	
Median time to first event (months) [a]	8.4	4.2	
95% Confidence Interval	[7.0, 11.3]	[2.9, 5.6]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.5935
95% Confidence Interval			[0.4609, 0.7641]
p-value			0.0001
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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#### Functional Scales/Role Functioning

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	217 (58.2)	106 (57.6)	
Number of subjects censored, n (%)	156 (41.8)	78 (42.4)	
Median time to first event (months) [a]	4.2	2.9	
95% Confidence Interval	[2.9, 5.7]	[1.5, 4.3]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.7648
95% Confidence Interval			[0.6032, 0.9698]
p-value			0.0269
Stratified log-rank p-value [c]			0.0257

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Functional Scales/Emotional Functioning

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	170 (45.6)	72 (39.1)	
Number of subjects censored, n (%)	203 (54.4)	112 (60.9)	
Median time to first event (months) [a]	11.1	6.9	
95% Confidence Interval	[8.5, 13.6]	[5.7, 10.2]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.8127
95% Confidence Interval			[0.6127, 1.0781]
p-value			0.1504
Stratified log-rank p-value [c]			0.1446

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Functional Scales/Cognitive Functioning

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	205 (55.0)	97 (52.7)	
Number of subjects censored, n (%)	168 (45.0)	87 (47.3)	
Median time to first event (months) [a]	6.2	4.4	
95% Confidence Interval	[4.7, 7.7]	[3.3, 6.3]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.7820
95% Confidence Interval			[0.6094, 1.0035]
p-value			0.0533
Stratified log-rank p-value [c]			0.0493

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Functional Scales/Social Functioning

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	211 (56.6)	107 (58.2)	
Number of subjects censored, n (%)	162 (43.4)	77 (41.8)	
Median time to first event (months) [a]	5.9	3.8	
95% Confidence Interval	[4.2, 9.7]	[2.7, 4.7]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.7183
95% Confidence Interval			[0.5656, 0.9123]
p-value			0.0067
Stratified log-rank p-value [c]			0.0064

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Symptom Scales/Fatigue

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	240 (64.3)	111 (60.3)	
Number of subjects censored, n (%)	133 (35.7)	73 (39.7)	
Median time to first event (months) [a]	4.2	2.3	
95% Confidence Interval	[2.8, 4.9]	[1.4, 3.1]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.7752
95% Confidence Interval			[0.6154, 0.9766]
p-value			0.0307
Stratified log-rank p-value [c]			0.0295

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Symptom Scales/Nausea and Vomiting

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	258 (69.2)	73 (39.7)	
Number of subjects censored, n (%)	115 (30.8)	111 (60.3)	
Median time to first event (months) [a]	1.5	8.2	
95% Confidence Interval	[1.4, 1.7]	[6.0, 9.8]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			2.0765
95% Confidence Interval			[1.5976, 2.6990]
p-value			<0.0001
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Symptom Scales/Pain

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	188 (50.4)	97 (52.7)	
Number of subjects censored, n (%)	185 (49.6)	87 (47.3)	
Median time to first event (months) [a]	9.2	4.4	
95% Confidence Interval	[7.1, 11.1]	[2.7, 6.1]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.6239
95% Confidence Interval			[0.4848, 0.8031]
p-value			0.0002
Stratified log-rank p-value [c]			0.0002

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Common Symptoms/Dyspnoea

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	164 (44.0)	74 (40.2)	
Number of subjects censored, n (%)	209 (56.0)	110 (59.8)	
Median time to first event (months) [a]	12.5	6.7	
95% Confidence Interval	[8.3, 20.9]	[5.1, 13.7]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.7950
95% Confidence Interval			[0.6003, 1.0528]
p-value			0.1094
Stratified log-rank p-value [c]			0.1092

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Common Symptoms/Insomnia

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	149 (39.9)	85 (46.2)	
Number of subjects censored, n (%)	224 (60.1)	99 (53.8)	
Median time to first event (months) [a]	16.0	5.4	
95% Confidence Interval	[10.6, 18.6]	[4.2, 7.0]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.5237
95% Confidence Interval			[0.3970, 0.6907]
p-value			<0.0001
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Common Symptoms/Appetite Loss

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	215 (57.6)	80 (43.5)	
Number of subjects censored, n (%)	158 (42.4)	104 (56.5)	
Median time to first event (months) [a]	5.1	6.5	
95% Confidence Interval	[3.5, 7.2]	[5.0, 9.8]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			1.1907
95% Confidence Interval			[0.9179, 1.5445]
p-value			0.1887
Stratified log-rank p-value [c]			0.1976

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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#### Common Symptoms/Constipation

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	219 (58.7)	82 (44.6)	
Number of subjects censored, n (%)	154 (41.3)	102 (55.4)	
Median time to first event (months) [a]	4.2	5.9	
95% Confidence Interval	[2.9, 5.6]	[4.4, 8.4]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			1.1240
95% Confidence Interval			[0.8682, 1.4551]
p-value			0.3749
Stratified log-rank p-value [c]			0.3794

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Common Symptoms/Diarrhea

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	173 (46.4)	56 (30.4)	
Number of subjects censored, n (%)	200 (53.6)	128 (69.6)	
Median time to first event (months) [a]	9.6	13.3	
95% Confidence Interval	[7.0, 16.1]	[9.0, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			1.4167
95% Confidence Interval			[1.0442, 1.9220]
p-value			0.0252
Stratified log-rank p-value [c]			0.0254

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Common Symptoms/Financial Difficulties

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	106 (28.4)	48 (26.1)	
Number of subjects censored, n (%)	267 (71.6)	136 (73.9)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	18.5 [11.3, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.7699 [0.5421, 1.0935] 0.1441
Stratified log-rank p-value [c]			0.1405

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Global Health Status

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.5496
HER2 IHC 1+	214	125 (58.4)	89 (41.6)	4.3 (2.8, 5.7)	107	58 (54.2)	49 (45.8)	4.2 (2.7, 5.9)	0.8777 (0.6416, 1.2005) 0.4142	0.4014
HER2 IHC 2+/ISH Negative	159	85 (53.5)	74 (46.5)	7.2 (4.2, 12.7)	77	41 (53.2)	36 (46.8)	3.7 (2.0, 7.7)	0.7405 (0.5076, 1.0803) 0.1190	0.1158

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Global Health Status

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.6031
1	221	133 (60.2)	88 (39.8)	4.2 (2.8, 5.7)	100	54 (54.0)	46 (46.0)	3.5 (1.7, 7.7)	0.8609 (0.6258, 1.1842) 0.3572	0.3519
>=2	151	76 (50.3)	75 (49.7)	6.9 (4.9, 13.1)	83	45 (54.2)	38 (45.8)	4.5 (2.8, 6.9)	0.7303 (0.5035, 1.0593) 0.0976	0.0931

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Global Health Status

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.8876
Yes	235	130 (55.3)	105 (44.7)	4.3 (2.9, 8.1)	118	61 (51.7)	57 (48.3)	4.0 (2.7, 6.9)	0.8139 (0.5982, 1.1073) 0.1898	0.1806	
No	98	60 (61.2)	38 (38.8)	5.7 (4.2, 8.5)	48	28 (58.3)	20 (41.7)	3.9 (1.7, 9.7)	0.8342 (0.5322, 1.3077) 0.4294	0.4300	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Global Health Status

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5479
<65	290	160 (55.2)	130 (44.8)	5.7 (4.2, 8.6)	136	69 (50.7)	67 (49.3)	4.2 (2.8, 5.9)	0.7932 (0.5963, 1.0553) 0.1117	0.1061	
>=65	83	50 (60.2)	33 (39.8)	3.4 (1.7, 5.8)	48	30 (62.5)	18 (37.5)	3.7 (1.5, 7.7)	0.9513 (0.6042, 1.4976) 0.8291	0.8262	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Global Health Status

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											0.9107
<75	359	202 (56.3)	157 (43.7)	5.2 (4.1, 7.2)	175	93 (53.1)	82 (46.9)	4.2 (2.8, 5.9)	0.8101 (0.6322, 1.0381) 0.0961	0.0904	
>=75	14	8 (57.1)	6 (42.9)	4.4 (1.6, NE)	9	6 (66.7)	3 (33.3)	3.7 (0.7, NE)	0.8214 (0.2838, 2.3779) 0.7168	0.7205	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Global Health Status

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.3688
White	176	88 (50.0)	88 (50.0)	6.3 (3.9, 14.4)	91	45 (49.5)	46 (50.5)	4.0 (2.7, 8.6)	0.7406 (0.5153, 1.0645) 0.1047	0.1018	
Non-White	197	122 (61.9)	75 (38.1)	4.7 (2.9, 5.9)	92	53 (57.6)	39 (42.4)	4.2 (2.0, 6.9)	0.8898 (0.6431, 1.2311) 0.4810	0.4698	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.5240
Asia	147	100 (68.0)	47 (32.0)	4.2 (2.8, 5.7)	66	40 (60.6)	26 (39.4)	2.4 (1.5, 5.9)	0.9217 (0.6374, 1.3329) 0.6649	0.6529	
North America	60	26 (43.3)	34 (56.7)	6.3 (2.3, NE)	33	16 (48.5)	17 (51.5)	3.7 (1.5, 8.6)	0.6184 (0.3271, 1.1691) 0.1391	0.1343	
Europe + Israel	166	84 (50.6)	82 (49.4)	5.9 (4.2, 12.7)	85	43 (50.6)	42 (49.4)	4.5 (3.1, 9.0)	0.7854 (0.5426, 1.1369) 0.2005	0.1959	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Global Health Status

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.7630
0	200	125 (62.5)	75 (37.5)	4.3 (2.9, 5.7)	105	57 (54.3)	48 (45.7)	3.5 (2.1, 5.4)	0.8465 (0.6177, 1.1601) 0.3001	0.2964	
1	173	85 (49.1)	88 (50.9)	7.6 (4.2, 14.4)	79	42 (53.2)	37 (46.8)	5.1 (2.4, 8.4)	0.7685 (0.5287, 1.1172) 0.1678	0.1606	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Global Health Status

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.1744
0	60	38 (63.3)	22 (36.7)	4.2 (2.7, 6.3)	34	19 (55.9)	15 (44.1)	4.5 (1.7, 5.9)	0.8528 (0.4893, 1.4864) 0.5744	0.5783
1	108	58 (53.7)	50 (46.3)	5.8 (2.8, 13.1)	51	23 (45.1)	28 (54.9)	7.7 (2.3, NE)	1.1165 (0.6884, 1.8111) 0.6551	0.6559
2	115	55 (47.8)	60 (52.2)	8.8 (4.3, NE)	54	32 (59.3)	22 (40.7)	3.7 (2.7, 6.9)	0.5448 (0.3480, 0.8529) 0.0079	0.0063

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Global Health Status

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	59 (65.6)	31 (34.4)	4.2 (2.8, 5.7)	45	25 (55.6)	20 (44.4)	2.8 (1.5, NE)	0.8811 (0.5499, 1.4118) 0.5988	0.5882

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.2514
PD	174	80 (46.0)	94 (54.0)	8.6 (4.7, 18.2)	85	42 (49.4)	43 (50.6)	5.3 (2.8, 7.5)	0.6639 (0.4548, 0.9691) 0.0338	0.0317
PR	48	34 (70.8)	14 (29.2)	2.8 (1.4, 7.9)	22	10 (45.5)	12 (54.5)	3.9 (1.5, NE)	1.2856 (0.6318, 2.6160) 0.4882	0.5128
SD	82	50 (61.0)	32 (39.0)	4.8 (2.8, 8.5)	55	36 (65.5)	19 (34.5)	2.8 (1.6, 5.1)	0.7147 (0.4636, 1.1019) 0.1284	0.1280

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Global Health Status

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.3376
Yes	37	20 (54.1)	17 (45.9)	5.7 (2.9, NE)	15	4 (26.7)	11 (73.3)	NE (0.9, NE)	1.2719 (0.4334, 3.7325)	0.6617	
No	336	190 (56.5)	146 (43.5)	4.8 (3.9, 6.9)	169	95 (56.2)	74 (43.8)	3.9 (2.8, 5.8)	0.7969 (0.6214, 1.0218)	0.0689	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Global Health Status

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.0352
Yes	24	14 (58.3)	10 (41.7)	8.8 (1.4, NE)	8	1 (12.5)	7 (87.5)	NE (1.7, NE)	4.1172 (0.5375, 31.5378) 0.1731	0.1401
No	349	196 (56.2)	153 (43.8)	4.8 (3.9, 6.9)	176	98 (55.7)	78 (44.3)	3.9 (2.7, 5.4)	0.7807 (0.6113, 0.9971) 0.0473	0.0441

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Global Health Status

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.4396
Normal Function	202	103 (51.0)	99 (49.0)	5.7 (4.2, 18.2)	87	44 (50.6)	43 (49.4)	4.2 (3.0, 5.9)	0.7668 (0.5361, 1.0968) 0.1460	0.1353	
Mild Impairment	123	80 (65.0)	43 (35.0)	3.9 (2.8, 5.7)	69	39 (56.5)	30 (43.5)	2.8 (1.7, 8.4)	0.8479 (0.5763, 1.2476) 0.4024	0.3955	
Moderate Impairment	41	23 (56.1)	18 (43.9)	5.7 (1.6, NE)	23	12 (52.2)	11 (47.8)	7.7 (1.4, NE)	1.1962 (0.5946, 2.4068) 0.6155	0.6129	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Global Health Status

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.4134
Normal Function	170	106 (62.4)	64 (37.6)	4.5 (2.8, 5.7)	98	56 (57.1)	42 (42.9)	4.5 (2.8, 7.5)	0.9156 (0.6611, 1.2682) 0.5959	0.5753	
Mild Impairment	195	102 (52.3)	93 (47.7)	5.8 (3.9, 8.8)	84	41 (48.8)	43 (51.2)	3.9 (2.0, 8.6)	0.7767 (0.5382, 1.1209) 0.1770	0.1741	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Global Health Status

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.2189
Yes	332	181 (54.5)	151 (45.5)	5.6 (4.2, 8.1)	157	83 (52.9)	74 (47.1)	3.7 (2.7, 7.0)	0.7814 (0.6013, 1.0156) 0.0651	0.0622	
No	41	29 (70.7)	12 (29.3)	2.8 (1.6, 6.3)	27	16 (59.3)	11 (40.7)	5.3 (1.5, 5.9)	1.1390 (0.6172, 2.1021) 0.6771	0.6862	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Global Health Status

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (IXRS)											0.9811
Positive	331	189 (57.1)	142 (42.9)	5.1 (4.1, 7.0)	163	86 (52.8)	77 (47.2)	4.0 (2.7, 6.9)	0.8223 (0.6360, 1.0632) 0.1356	0.1299	
Negative	42	21 (50.0)	21 (50.0)	4.7 (2.2, NE)	21	13 (61.9)	8 (38.1)	4.4 (1.7, NE)	0.7858 (0.3894, 1.5858) 0.5010	0.5013	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Global Health Status

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.8760
Positive	333	190 (57.1)	143 (42.9)	5.1 (4.1, 7.0)	166	89 (53.6)	77 (46.4)	4.0 (2.7, 5.9)	0.8149 (0.6322, 1.0504)	0.1084	
Negative	40	20 (50.0)	20 (50.0)	4.7 (2.7, NE)	18	10 (55.6)	8 (44.4)	5.3 (1.7, NE)	0.8348 (0.3866, 1.8027)	0.6439	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.3181
HER2 IHC 1+	214	108 (50.5)	106 (49.5)	8.7 (6.3, 11.3)	107	54 (50.5)	53 (49.5)	4.5 (3.0, 8.5)	0.6723 (0.4809, 0.9399) 0.0202	0.0187
HER2 IHC 2+/ISH Negative	159	79 (49.7)	80 (50.3)	8.2 (6.7, 15.2)	77	45 (58.4)	32 (41.6)	3.1 (1.8, 5.9)	0.4933 (0.3377, 0.7207) 0.0003	0.0002

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.9682
1	221	111 (50.2)	110 (49.8)	9.0 (7.0, 11.5)	100	54 (54.0)	46 (46.0)	4.3 (2.2, 6.5)	0.5835 (0.4172, 0.8160) 0.0016	0.0014
>=2	151	76 (50.3)	75 (49.7)	7.5 (5.6, 16.6)	83	45 (54.2)	38 (45.8)	4.2 (2.3, 6.1)	0.5999 (0.4110, 0.8757) 0.0081	0.0073

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Prior CDK4/6											
Yes	235	116 (49.4)	119 (50.6)	8.4 (6.4, 11.3)	118	59 (50.0)	59 (50.0)	4.5 (3.0, 7.7)	0.6567 (0.4761, 0.9059) 0.0104	0.0093	0.2710
No	98	52 (53.1)	46 (46.9)	9.6 (5.9, 16.6)	48	30 (62.5)	18 (37.5)	3.0 (1.5, 6.1)	0.4813 (0.3026, 0.7656) 0.0020	0.0016	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7752
<65	290	144 (49.7)	146 (50.3)	8.3 (7.1, 11.3)	136	71 (52.2)	65 (47.8)	4.2 (2.9, 5.8)	0.5791 (0.4315, 0.7772) 0.0003	0.0002	
>=65	83	43 (51.8)	40 (48.2)	10.2 (4.9, 15.2)	48	28 (58.3)	20 (41.7)	4.5 (1.4, 9.5)	0.6271 (0.3864, 1.0177) 0.0589	0.0573	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6688
<75	359	181 (50.4)	178 (49.6)	8.3 (7.0, 11.3)	175	92 (52.6)	83 (47.4)	4.3 (2.9, 5.8)	0.5965 (0.4605, 0.7727) 0.0001	<0.0001	
>=75	14	6 (42.9)	8 (57.1)	11.5 (2.8, NE)	9	7 (77.8)	2 (22.2)	3.1 (0.7, 11.4)	0.4659 (0.1555, 1.3963) 0.1726	0.1574	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.8888
White	176	84 (47.7)	92 (52.3)	9.0 (6.2, 11.5)	91	46 (50.5)	45 (49.5)	4.2 (2.3, 5.3)	0.5627 (0.3880, 0.8161) 0.0024	0.0021	
Non-White	197	103 (52.3)	94 (47.7)	8.2 (6.7, 13.4)	92	53 (57.6)	39 (42.4)	4.2 (1.7, 6.1)	0.6021 (0.4286, 0.8459) 0.0035	0.0030	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.8915
Asia	147	84 (57.1)	63 (42.9)	7.8 (5.9, 11.3)	66	39 (59.1)	27 (40.9)	4.2 (1.5, 5.9)	0.6267 (0.4245, 0.9251) 0.0187	0.0174	
North America	60	24 (40.0)	36 (60.0)	9.9 (4.9, NE)	33	14 (42.4)	19 (57.6)	4.5 (1.4, NE)	0.5399 (0.2738, 1.0648) 0.0753	0.0720	
Europe + Israel	166	79 (47.6)	87 (52.4)	9.1 (6.2, 12.5)	85	46 (54.1)	39 (45.9)	4.2 (2.3, 7.5)	0.5828 (0.4011, 0.8468) 0.0046	0.0039	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.4507
0	200	96 (48.0)	104 (52.0)	9.9 (7.7, 16.6)	105	52 (49.5)	53 (50.5)	4.2 (2.1, 7.7)	0.5487 (0.3877, 0.7766) 0.0007	0.0006	
1	173	91 (52.6)	82 (47.4)	6.8 (5.2, 11.3)	79	47 (59.5)	32 (40.5)	4.5 (2.3, 5.6)	0.6396 (0.4447, 0.9201) 0.0160	0.0141	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.5284
0	60	32 (53.3)	28 (46.7)	7.4 (5.4, 11.3)	34	18 (52.9)	16 (47.1)	3.1 (0.9, 5.9)	0.5332 (0.2930, 0.9703) 0.0395	0.0365	
1	108	46 (42.6)	62 (57.4)	11.3 (7.5, NE)	51	30 (58.8)	21 (41.2)	4.3 (2.3, 6.5)	0.4877 (0.3045, 0.7813) 0.0028	0.0023	
2	115	54 (47.0)	61 (53.0)	11.5 (5.9, NE)	54	27 (50.0)	27 (50.0)	4.5 (2.0, 9.7)	0.5665 (0.3501, 0.9165) 0.0206	0.0174	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	55 (61.1)	35 (38.9)	6.7 (2.9, 8.7)	45	24 (53.3)	21 (46.7)	4.2 (1.5, 10.1)	0.8254 (0.5066, 1.3448) 0.4410	0.4366	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.2385
PD	174	82 (47.1)	92 (52.9)	9.1 (7.2, 13.4)	85	38 (44.7)	47 (55.3)	5.9 (4.2, 8.5)	0.6284 (0.4240, 0.9315) 0.0207	0.0195	
PR	48	29 (60.4)	19 (39.6)	5.8 (1.6, 11.3)	22	10 (45.5)	12 (54.5)	4.3 (1.4, NE)	0.9183 (0.4427, 1.9047) 0.8189	0.8054	
SD	82	42 (51.2)	40 (48.8)	9.9 (4.9, 21.7)	55	38 (69.1)	17 (30.9)	2.9 (1.5, 4.5)	0.4876 (0.3065, 0.7757) 0.0024	0.0018	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.9802
Yes	37	19 (51.4)	18 (48.6)	8.3 (2.8, NE)	15	6 (40.0)	9 (60.0)	1.5 (0.8, NE)	0.6712 (0.2625, 1.7162) 0.4052	0.4046	
No	336	168 (50.0)	168 (50.0)	8.5 (7.0, 11.3)	169	93 (55.0)	76 (45.0)	4.3 (3.0, 5.6)	0.5840 (0.4500, 0.7580) 0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.8599
Yes	24	14 (58.3)	10 (41.7)	5.4 (0.9, NE)	8	4 (50.0)	4 (50.0)	1.0 (0.7, NE)	0.6426 (0.2047, 2.0170) 0.4486	0.4575
No	349	173 (49.6)	176 (50.4)	8.5 (7.1, 11.3)	176	95 (54.0)	81 (46.0)	4.3 (3.0, 5.6)	0.5822 (0.4500, 0.7532) <0.0001	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.1462
Normal Function	202	96 (47.5)	106 (52.5)	9.2 (7.3, 18.1)	87	50 (57.5)	37 (42.5)	3.9 (1.6, 4.6)	0.4775 (0.3350, 0.6806) <0.0001	<0.0001	
Mild Impairment	123	64 (52.0)	59 (48.0)	8.2 (5.2, 12.5)	69	34 (49.3)	35 (50.7)	5.6 (2.0, 7.5)	0.6553 (0.4248, 1.0109) 0.0560	0.0532	
Moderate Impairment	41	24 (58.5)	17 (41.5)	7.7 (3.4, 16.6)	23	13 (56.5)	10 (43.5)	5.9 (1.6, NE)	0.9560 (0.4849, 1.8848) 0.8967	0.8892	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.4086
Normal Function	170	90 (52.9)	80 (47.1)	9.2 (5.8, 12.5)	98	58 (59.2)	40 (40.8)	3.0 (1.5, 5.6)	0.5467 (0.3889, 0.7684) 0.0005	0.0004	
Mild Impairment	195	95 (48.7)	100 (51.3)	8.2 (6.7, 11.5)	84	41 (48.8)	43 (51.2)	4.5 (3.1, 7.7)	0.6353 (0.4360, 0.9257) 0.0182	0.0168	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.0653
Yes	332	168 (50.6)	164 (49.4)	8.1 (6.7, 11.3)	157	80 (51.0)	77 (49.0)	4.5 (3.0, 6.5)	0.6438 (0.4902, 0.8454) 0.0015	0.0013	
No	41	19 (46.3)	22 (53.7)	10.2 (7.2, NE)	27	19 (70.4)	8 (29.6)	1.6 (1.3, 4.6)	0.3559 (0.1779, 0.7120) 0.0035	0.0023	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.4923
Positive	331	166 (50.2)	165 (49.8)	8.5 (7.0, 11.3)	163	85 (52.1)	78 (47.9)	4.5 (3.0, 6.1)	0.6077 (0.4646, 0.7949) 0.0003	0.0002	
Negative	42	21 (50.0)	21 (50.0)	7.4 (2.8, NE)	21	14 (66.7)	7 (33.3)	1.8 (0.9, 5.3)	0.4901 (0.2428, 0.9891) 0.0465	0.0418	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.8939
Positive	333	167 (50.2)	166 (49.8)	8.5 (7.0, 11.3)	166	89 (53.6)	77 (46.4)	4.2 (2.9, 5.8)	0.5918 (0.4543, 0.7710) 0.0001	<0.0001	
Negative	40	20 (50.0)	20 (50.0)	7.8 (2.9, NE)	18	10 (55.6)	8 (44.4)	4.5 (0.8, NE)	0.5811 (0.2656, 1.2716) 0.1743	0.1682	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.2945
HER2 IHC 1+	214	121 (56.5)	93 (43.5)	4.3 (2.8, 5.9)	107	62 (57.9)	45 (42.1)	2.9 (1.4, 4.3)	0.6636 (0.4866, 0.9051) 0.0096	0.0093	
HER2 IHC 2+/ISH Negative	159	96 (60.4)	63 (39.6)	4.2 (2.8, 6.3)	77	44 (57.1)	33 (42.9)	2.9 (1.5, 6.1)	0.8454 (0.5901, 1.2112) 0.3600	0.3520	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.7569
1	221	134 (60.6)	87 (39.4)	4.2 (2.8, 5.6)	100	59 (59.0)	41 (41.0)	2.1 (1.4, 4.3)	0.7598 (0.5585, 1.0338) 0.0804	0.0795
>=2	151	82 (54.3)	69 (45.7)	5.6 (2.8, 8.4)	83	47 (56.6)	36 (43.4)	2.9 (1.6, 4.7)	0.6965 (0.4834, 1.0036) 0.0523	0.0488

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.3747
Yes	235	133 (56.6)	102 (43.4)	4.2 (2.9, 6.2)	118	65 (55.1)	53 (44.9)	2.9 (1.5, 4.4)	0.7678 (0.5693, 1.0357) 0.0835	0.0798	
No	98	62 (63.3)	36 (36.7)	5.1 (2.8, 7.5)	48	32 (66.7)	16 (33.3)	1.5 (1.2, 4.3)	0.5960 (0.3867, 0.9183) 0.0190	0.0185	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3618
<65	290	160 (55.2)	130 (44.8)	4.6 (3.5, 6.9)	136	75 (55.1)	61 (44.9)	3.2 (1.5, 4.4)	0.6988 (0.5292, 0.9227) 0.0115	0.0108	
>=65	83	57 (68.7)	26 (31.3)	2.8 (1.5, 4.2)	48	31 (64.6)	17 (35.4)	1.9 (1.4, 4.7)	0.8901 (0.5731, 1.3823) 0.6042	0.6085	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8785
<75	359	209 (58.2)	150 (41.8)	4.3 (2.9, 5.8)	175	100 (57.1)	75 (42.9)	2.9 (1.5, 4.4)	0.7320 (0.5753, 0.9315) 0.0112	0.0105	
>=75	14	8 (57.1)	6 (42.9)	2.8 (1.6, NE)	9	6 (66.7)	3 (33.3)	2.8 (0.7, NE)	0.8068 (0.2794, 2.3302) 0.6916	0.6757	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.1981
White	176	99 (56.3)	77 (43.8)	2.9 (2.8, 5.6)	91	46 (50.5)	45 (49.5)	3.8 (1.5, 4.8)	0.8927 (0.6278, 1.2692)	0.5229 (0.5272)	
Non-White	197	118 (59.9)	79 (40.1)	4.6 (3.3, 6.7)	92	60 (65.2)	32 (34.8)	2.0 (1.4, 3.7)	0.6222 (0.4543, 0.8523)	0.0028 (0.0031)	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.2350
Asia	147	90 (61.2)	57 (38.8)	4.6 (4.2, 6.9)	66	46 (69.7)	20 (30.3)	2.1 (1.4, 4.4)	0.6092 (0.4253, 0.8726) 0.0069	0.0064	
North America	60	27 (45.0)	33 (55.0)	4.1 (1.6, NE)	33	17 (51.5)	16 (48.5)	2.0 (1.4, 4.5)	0.6687 (0.3608, 1.2391) 0.2010	0.1943	
Europe + Israel	166	100 (60.2)	66 (39.8)	2.9 (2.8, 5.9)	85	43 (50.6)	42 (49.4)	3.8 (1.5, 5.8)	0.9416 (0.6574, 1.3486) 0.7427	0.7332	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.8635
0	200	118 (59.0)	82 (41.0)	4.3 (2.9, 6.3)	105	58 (55.2)	47 (44.8)	2.8 (1.5, 4.5)	0.7272 (0.5298, 0.9982) 0.0487	0.0474	
1	173	99 (57.2)	74 (42.8)	4.2 (2.8, 6.2)	79	48 (60.8)	31 (39.2)	2.9 (1.5, 4.5)	0.7472 (0.5268, 1.0600) 0.1024	0.0987	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.2458
0	60	40 (66.7)	20 (33.3)	2.8 (1.4, 3.3)	34	17 (50.0)	17 (50.0)	4.5 (1.5, 5.9)	1.0841 (0.6113, 1.9226) 0.7824	0.7835	
1	108	57 (52.8)	51 (47.2)	4.4 (2.8, 12.5)	51	28 (54.9)	23 (45.1)	3.2 (1.4, 6.1)	0.7725 (0.4910, 1.2154) 0.2643	0.2594	
2	115	60 (52.2)	55 (47.8)	5.9 (4.2, 11.8)	54	33 (61.1)	21 (38.9)	2.1 (1.4, 3.7)	0.5439 (0.3516, 0.8414) 0.0062	0.0050	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	60 (66.7)	30 (33.3)	3.3 (1.6, 5.6)	45	28 (62.2)	17 (37.8)	1.5 (0.9, 6.7)	0.7718 (0.4894, 1.2171) 0.2651	0.2646

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.7732
PD	174	91 (52.3)	83 (47.7)	4.4 (2.9, 7.2)	85	44 (51.8)	41 (48.2)	3.2 (1.5, 4.7)	0.7219 (0.5015, 1.0392) 0.0796	0.0780	
PR	48	30 (62.5)	18 (37.5)	4.3 (2.8, 16.4)	22	11 (50.0)	11 (50.0)	5.8 (0.8, NE)	0.9223 (0.4588, 1.8541) 0.8205	0.8052	
SD	82	51 (62.2)	31 (37.8)	4.2 (1.7, 6.7)	55	36 (65.5)	19 (34.5)	2.9 (1.4, 4.5)	0.7301 (0.4738, 1.1249) 0.1538	0.1536	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.0222
Yes	37	24 (64.9)	13 (35.1)	2.3 (1.4, 5.9)	15	4 (26.7)	11 (73.3)	NE (1.0, NE)	2.1490 (0.7445, 6.2026) 0.1572	0.1440	
No	336	193 (57.4)	143 (42.6)	4.3 (2.9, 6.2)	169	102 (60.4)	67 (39.6)	2.8 (1.5, 4.2)	0.6773 (0.5313, 0.8633) 0.0017	0.0015	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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## Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0030
Yes	24	16 (66.7)	8 (33.3)	1.6 (0.9, 5.9)	8	1 (12.5)	7 (87.5)	NE (0.7, NE)	6.1059 (0.8076, 46.1641) 0.0796	0.0430	
No	349	201 (57.6)	148 (42.4)	4.3 (2.9, 5.9)	176	105 (59.7)	71 (40.3)	2.8 (1.5, 3.8)	0.6798 (0.5354, 0.8632) 0.0015	0.0014	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.3335
Normal Function	202	112 (55.4)	90 (44.6)	4.4 (2.9, 7.5)	87	49 (56.3)	38 (43.7)	2.8 (1.5, 4.2)	0.6484 (0.4613, 0.9115) 0.0127	0.0116	
Mild Impairment	123	76 (61.8)	47 (38.2)	4.1 (2.8, 5.7)	69	41 (59.4)	28 (40.6)	2.9 (1.4, 4.7)	0.7965 (0.5419, 1.1708) 0.2470	0.2447	
Moderate Impairment	41	25 (61.0)	16 (39.0)	2.9 (1.6, 16.6)	23	12 (52.2)	11 (47.8)	5.9 (1.4, NE)	1.1270 (0.5652, 2.2473) 0.7342	0.7380	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1473
Normal Function	170	111 (65.3)	59 (34.7)	2.9 (2.8, 4.3)	98	56 (57.1)	42 (42.9)	2.9 (1.5, 5.8)	0.8993 (0.6510, 1.2423) 0.5196	0.5126	
Mild Impairment	195	104 (53.3)	91 (46.7)	5.6 (4.2, 7.5)	84	48 (57.1)	36 (42.9)	2.9 (1.5, 4.2)	0.6043 (0.4264, 0.8564) 0.0046	0.0041	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.8795
Yes	332	190 (57.2)	142 (42.8)	4.2 (2.9, 5.9)	157	90 (57.3)	67 (42.7)	2.9 (1.5, 4.4)	0.7501 (0.5827, 0.9657) 0.0257	0.0252	
No	41	27 (65.9)	14 (34.1)	2.9 (1.5, 7.7)	27	16 (59.3)	11 (40.7)	2.8 (1.5, 5.8)	0.6270 (0.3251, 1.2092) 0.1636	0.1522	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.7289
Positive	331	193 (58.3)	138 (41.7)	4.3 (2.9, 5.9)	163	93 (57.1)	70 (42.9)	2.9 (1.5, 4.3)	0.7249 (0.5646, 0.9307) 0.0116	0.0111	
Negative	42	24 (57.1)	18 (42.9)	2.8 (1.4, 5.9)	21	13 (61.9)	8 (38.1)	3.4 (1.0, 5.9)	0.8914 (0.4528, 1.7546) 0.7393	0.7325	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.2997
Positive	333	194 (58.3)	139 (41.7)	4.3 (2.9, 5.9)	166	97 (58.4)	69 (41.6)	2.8 (1.5, 4.2)	0.7060 (0.5519, 0.9032) 0.0056	0.0053	
Negative	40	23 (57.5)	17 (42.5)	2.8 (1.4, 5.9)	18	9 (50.0)	9 (50.0)	4.5 (1.4, NE)	1.1462 (0.5293, 2.4822) 0.7292	0.7345	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.4553
HER2 IHC 1+	214	105 (49.1)	109 (50.9)	9.9 (7.9, 11.8)	107	46 (43.0)	61 (57.0)	6.3 (4.7, 7.9)	0.6992 (0.4893, 0.9991)	0.0476
HER2 IHC 2+/ISH Negative	159	65 (40.9)	94 (59.1)	21.7 (9.7, NE)	77	26 (33.8)	51 (66.2)	14.8 (5.7, NE)	0.9778 (0.6184, 1.5461)	0.9155

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.7000
1	221	109 (49.3)	112 (50.7)	10.4 (7.2, 13.1)	100	43 (43.0)	57 (57.0)	6.3 (5.6, 7.9)	0.8485 (0.5929, 1.2144) 0.3691	0.3617
>=2	151	61 (40.4)	90 (59.6)	11.3 (9.7, NE)	83	29 (34.9)	54 (65.1)	7.0 (5.3, NE)	0.7634 (0.4864, 1.1983) 0.2406	0.2383

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.4079
Yes	235	104 (44.3)	131 (55.7)	11.2 (8.3, 17.0)	118	41 (34.7)	77 (65.3)	7.0 (5.6, NE)	0.9082 (0.6297, 1.3098) 0.6061	0.5993	
No	98	48 (49.0)	50 (51.0)	11.1 (7.9, NE)	48	23 (47.9)	25 (52.1)	6.3 (5.6, 11.7)	0.6819 (0.4110, 1.1313) 0.1382	0.1342	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9532
<65	290	132 (45.5)	158 (54.5)	11.1 (9.2, 15.2)	136	52 (38.2)	84 (61.8)	6.3 (5.7, 10.2)	0.8024 (0.5787, 1.1126) 0.1867	0.1827	
>=65	83	38 (45.8)	45 (54.2)	9.9 (5.9, NE)	48	20 (41.7)	28 (58.3)	7.7 (4.4, NE)	0.8432 (0.4869, 1.4602) 0.5428	0.5426	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6662
<75	359	163 (45.4)	196 (54.6)	11.1 (8.5, 15.2)	175	68 (38.9)	107 (61.1)	6.9 (5.7, 10.2)	0.7967 (0.5972, 1.0628) 0.1221	0.1190	
>=75	14	7 (50.0)	7 (50.0)	9.9 (2.1, NE)	9	4 (44.4)	5 (55.6)	NE (0.7, NE)	1.1355 (0.3313, 3.8911) 0.8398	0.8212	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Race										0.9522
White	176	81 (46.0)	95 (54.0)	10.3 (7.1, 19.2)	91	35 (38.5)	56 (61.5)	5.9 (4.5, 10.2)	0.8228 (0.5490, 1.2333) 0.3449	0.3392
Non-White	197	89 (45.2)	108 (54.8)	11.8 (8.3, NE)	92	37 (40.2)	55 (59.8)	7.0 (5.7, 14.8)	0.7931 (0.5373, 1.1707) 0.2433	0.2436

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Region										0.8919
Asia	147	68 (46.3)	79 (53.7)	12.4 (8.3, NE)	66	26 (39.4)	40 (60.6)	7.1 (5.7, NE)	0.8308 (0.5258, 1.3129) 0.4273	0.4277
North America	60	22 (36.7)	38 (63.3)	19.2 (2.9, NE)	33	11 (33.3)	22 (66.7)	6.3 (2.0, NE)	0.7733 (0.3687, 1.6219) 0.4963	0.4933
Europe + Israel	166	80 (48.2)	86 (51.8)	10.2 (6.8, 15.2)	85	35 (41.2)	50 (58.8)	5.9 (4.4, 11.7)	0.8348 (0.5569, 1.2512) 0.3818	0.3753

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	200	92 (46.0)	108 (54.0)	11.8 (8.3, 21.7)	105	38 (36.2)	67 (63.8)	7.1 (5.6, 14.8)	0.8402 (0.5728, 1.2326) 0.3733	0.3680	0.8607
1	173	78 (45.1)	95 (54.9)	10.4 (7.2, 13.6)	79	34 (43.0)	45 (57.0)	6.9 (4.4, NE)	0.7672 (0.5077, 1.1593) 0.2083	0.2057	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.5722
0	60	29 (48.3)	31 (51.7)	9.7 (4.1, NE)	34	13 (38.2)	21 (61.8)	5.6 (3.0, NE)	0.8730 (0.4501, 1.6932) 0.6878	0.6884	
1	108	49 (45.4)	59 (54.6)	11.1 (7.1, 21.7)	51	22 (43.1)	29 (56.9)	6.3 (5.7, NE)	0.8690 (0.5227, 1.4446) 0.5881	0.5820	
2	115	55 (47.8)	60 (52.2)	10.5 (7.1, NE)	54	25 (46.3)	29 (53.7)	6.3 (3.7, 7.9)	0.6138 (0.3757, 1.0026) 0.0512	0.0487	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	37 (41.1)	53 (58.9)	15.2 (9.7, NE)	45	12 (26.7)	33 (73.3)	NE (5.7, NE)	1.1030 (0.5697, 2.1354) 0.7713	0.7684

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.5971
PD	174	78 (44.8)	96 (55.2)	10.3 (7.1, 17.0)	85	31 (36.5)	54 (63.5)	6.9 (5.3, NE)	0.8755 (0.5728, 1.3382) 0.5390	0.5315	
PR	48	22 (45.8)	26 (54.2)	12.5 (10.2, NE)	22	8 (36.4)	14 (63.6)	11.7 (3.1, NE)	0.6526 (0.2838, 1.5010) 0.3153	0.3191	
SD	82	32 (39.0)	50 (61.0)	19.2 (8.4, NE)	55	25 (45.5)	30 (54.5)	5.9 (4.7, NE)	0.6176 (0.3624, 1.0524) 0.0764	0.0734	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.4936
Yes	37	16 (43.2)	21 (56.8)	12.5 (7.1, NE)	15	3 (20.0)	12 (80.0)	NE (5.9, NE)	1.0503 (0.2985, 3.6948) 0.9391	0.9391	
No	336	154 (45.8)	182 (54.2)	10.5 (8.4, 15.2)	169	69 (40.8)	100 (59.2)	6.9 (5.6, 10.2)	0.8073 (0.6049, 1.0773) 0.1459	0.1424	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.2819
Yes	24	11 (45.8)	13 (54.2)	9.7 (4.2, NE)	8	2 (25.0)	6 (75.0)	NE (4.7, NE)	1.5246 (0.3343, 6.9527) 0.5860	0.5833	
No	349	159 (45.6)	190 (54.4)	11.1 (8.5, 15.2)	176	70 (39.8)	106 (60.2)	6.9 (5.7, 10.2)	0.7920 (0.5949, 1.0543) 0.1102	0.1073	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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## Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Renal function at baseline										0.2795
Normal Function	202	97 (48.0)	105 (52.0)	10.2 (7.5, 13.6)	87	33 (37.9)	54 (62.1)	6.3 (5.3, NE)	0.8235 (0.5503, 1.2323) 0.3450	0.3409
Mild Impairment	123	51 (41.5)	72 (58.5)	12.5 (8.3, NE)	69	29 (42.0)	40 (58.0)	6.1 (4.4, 10.2)	0.6234 (0.3885, 1.0004) 0.0502	0.0468
Moderate Impairment	41	21 (51.2)	20 (48.8)	9.9 (3.4, NE)	23	9 (39.1)	14 (60.9)	NE (1.4, NE)	1.2971 (0.5927, 2.8385) 0.5150	0.5079

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.1126
Normal Function	170	79 (46.5)	91 (53.5)	12.5 (8.5, 19.2)	98	46 (46.9)	52 (53.1)	6.3 (4.7, 7.7)	0.6543 (0.4513, 0.9485) 0.0251	0.0233
Mild Impairment	195	91 (46.7)	104 (53.3)	9.7 (7.1, 13.1)	84	26 (31.0)	58 (69.0)	10.2 (5.3, NE)	1.0622 (0.6831, 1.6516) 0.7888	0.7888

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline visceral disease										0.2925
Yes	332	148 (44.6)	184 (55.4)	11.1 (9.7, 15.2)	157	57 (36.3)	100 (63.7)	7.1 (6.1, 14.8)	0.8625 (0.6328, 1.1757) 0.3495	0.3447
No	41	22 (53.7)	19 (46.3)	7.1 (1.6, NE)	27	15 (55.6)	12 (44.4)	4.7 (1.5, 5.9)	0.6945 (0.3531, 1.3660) 0.2909	0.2823

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.6683
Positive	331	151 (45.6)	180 (54.4)	11.1 (8.5, 15.2)	163	63 (38.7)	100 (61.3)	7.0 (5.7, 11.7)	0.8182 (0.6070, 1.1030) 0.1879	0.1839	
Negative	42	19 (45.2)	23 (54.8)	12.5 (2.8, NE)	21	9 (42.9)	12 (57.1)	5.3 (1.4, NE)	0.7924 (0.3517, 1.7853) 0.5745	0.5780	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (derived)										0.6873
Positive	333	151 (45.3)	182 (54.7)	11.1 (9.2, 17.0)	166	64 (38.6)	102 (61.4)	7.0 (5.7, 11.7)	0.8141 (0.6048, 1.0958) 0.1750	0.1712
Negative	40	19 (47.5)	21 (52.5)	12.5 (2.8, NE)	18	8 (44.4)	10 (55.6)	5.3 (1.1, NE)	0.7679 (0.3304, 1.7846) 0.5393	0.5431

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.6597
HER2 IHC 1+	214	113 (52.8)	101 (47.2)	5.7 (4.2, 9.7)	107	56 (52.3)	51 (47.7)	4.3 (3.2, 6.9)	0.7492 (0.5410, 1.0376) 0.0822	0.0788
HER2 IHC 2+/ISH Negative	159	92 (57.9)	67 (42.1)	7.0 (4.4, 8.1)	77	41 (53.2)	36 (46.8)	5.3 (2.8, 8.6)	0.8416 (0.5800, 1.2212) 0.3639	0.3502

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.5114
1	221	127 (57.5)	94 (42.5)	5.0 (3.7, 7.0)	100	57 (57.0)	43 (43.0)	4.2 (2.8, 6.3)	0.8630 (0.6302, 1.1819) 0.3584	0.3473
>=2	151	78 (51.7)	73 (48.3)	8.1 (5.6, 12.5)	83	40 (48.2)	43 (51.8)	5.9 (3.9, 8.5)	0.6607 (0.4449, 0.9811) 0.0399	0.0374

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Prior CDK4/6										0.7252
Yes	235	127 (54.0)	108 (46.0)	6.2 (4.4, 8.4)	118	63 (53.4)	55 (46.6)	4.2 (2.8, 6.3)	0.7271 (0.5352, 0.9879) 0.0416	0.0382
No	98	55 (56.1)	43 (43.9)	6.9 (3.5, 14.7)	48	25 (52.1)	23 (47.9)	5.8 (3.5, 11.3)	0.8418 (0.5213, 1.3593) 0.4811	0.4745

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6204
<65	290	164 (56.6)	126 (43.4)	5.9 (4.4, 7.7)	136	71 (52.2)	65 (47.8)	4.4 (3.9, 6.1)	0.7896 (0.5951, 1.0478) 0.1018	0.0950	
>=65	83	41 (49.4)	42 (50.6)	7.0 (3.7, 17.0)	48	26 (54.2)	22 (45.8)	4.2 (1.5, 11.3)	0.6960 (0.4212, 1.1503) 0.1574	0.1561	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6918
<75	359	199 (55.4)	160 (44.6)	5.9 (4.4, 7.7)	175	92 (52.6)	83 (47.4)	4.2 (3.1, 5.9)	0.7648 (0.5950, 0.9832) 0.0364	0.0336	
>=75	14	6 (42.9)	8 (57.1)	14.1 (1.6, NE)	9	5 (55.6)	4 (44.4)	11.1 (0.8, NE)	0.9266 (0.2814, 3.0514) 0.9002	0.9002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.6147
White	176	95 (54.0)	81 (46.0)	6.2 (4.4, 9.9)	91	48 (52.7)	43 (47.3)	3.9 (2.8, 5.8)	0.7115 (0.4992, 1.0142) 0.0598	0.0555	
Non-White	197	110 (55.8)	87 (44.2)	6.5 (4.2, 8.4)	92	49 (53.3)	43 (46.7)	5.8 (4.2, 8.5)	0.8391 (0.5972, 1.1790) 0.3121	0.3051	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.0993
Asia	147	90 (61.2)	57 (38.8)	5.0 (4.1, 7.5)	66	39 (59.1)	27 (40.9)	5.8 (1.7, 8.5)	0.8571 (0.5871, 1.2512) 0.4243	0.4176	
North America	60	28 (46.7)	32 (53.3)	5.6 (1.6, 12.5)	33	8 (24.2)	25 (75.8)	7.9 (4.4, NE)	1.5051 (0.6781, 3.3410) 0.3149	0.3132	
Europe + Israel	166	87 (52.4)	79 (47.6)	7.1 (5.6, 11.8)	85	50 (58.8)	35 (41.2)	3.2 (2.7, 5.7)	0.6036 (0.4222, 0.8628) 0.0056	0.0048	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.8108
0	200	110 (55.0)	90 (45.0)	7.0 (5.0, 11.1)	105	52 (49.5)	53 (50.5)	5.3 (2.8, 7.9)	0.7639 (0.5468, 1.0673) 0.1146	0.1114	
1	173	95 (54.9)	78 (45.1)	5.4 (3.5, 8.1)	79	45 (57.0)	34 (43.0)	4.2 (3.1, 7.0)	0.7931 (0.5528, 1.1378) 0.2080	0.1979	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.7191
0	60	40 (66.7)	20 (33.3)	4.2 (2.2, 5.6)	34	18 (52.9)	16 (47.1)	5.6 (1.5, 9.0)	0.9845 (0.5602, 1.7302)	0.9510 0.9566
1	108	53 (49.1)	55 (50.9)	7.5 (4.2, 13.1)	51	28 (54.9)	23 (45.1)	5.8 (3.0, 11.1)	0.8148 (0.5139, 1.2918)	0.3688 0.3837
2	115	62 (53.9)	53 (46.1)	7.0 (4.4, 12.7)	54	26 (48.1)	28 (51.9)	4.2 (2.8, 8.5)	0.6955 (0.4331, 1.1167)	0.1280 0.1328

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	50 (55.6)	40 (44.4)	6.9 (4.2, 16.0)	45	25 (55.6)	20 (44.4)	4.2 (1.5, 5.8)	0.7081 (0.4343, 1.1545) 0.1664	0.1621

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.1756
PD	174	85 (48.9)	89 (51.1)	7.1 (5.6, 13.9)	85	39 (45.9)	46 (54.1)	5.8 (3.3, 6.9)	0.7374 (0.4999, 1.0878) 0.1246	0.1197	
PR	48	25 (52.1)	23 (47.9)	7.7 (4.2, NE)	22	15 (68.2)	7 (31.8)	3.6 (0.8, 8.6)	0.4990 (0.2606, 0.9555) 0.0360	0.0301	
SD	82	53 (64.6)	29 (35.4)	4.2 (2.4, 7.0)	55	32 (58.2)	23 (41.8)	4.4 (2.3, 9.3)	1.0355 (0.6656, 1.6109) 0.8771	0.8808	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.4923
Yes	37	20 (54.1)	17 (45.9)	7.2 (3.7, NE)	15	5 (33.3)	10 (66.7)	8.5 (1.4, NE)	1.0510 (0.3881, 2.8463) 0.9220	0.9241	
No	336	185 (55.1)	151 (44.9)	6.0 (4.4, 7.7)	169	92 (54.4)	77 (45.6)	4.2 (3.2, 5.9)	0.7690 (0.5968, 0.9909) 0.0423	0.0394	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.2562
Yes	24	15 (62.5)	9 (37.5)	7.2 (1.6, NE)	8	3 (37.5)	5 (62.5)	8.5 (1.7, NE)	1.3588 (0.3881, 4.7568)	0.6300	
No	349	190 (54.4)	159 (45.6)	6.2 (4.4, 7.7)	176	94 (53.4)	82 (46.6)	4.2 (3.2, 5.9)	0.7658 (0.5960, 0.9839)	0.0340	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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## Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.6020
Normal Function	202	110 (54.5)	92 (45.5)	7.1 (5.3, 10.4)	87	48 (55.2)	39 (44.8)	4.2 (3.0, 5.7)	0.6876 (0.4867, 0.9713) 0.0336	0.0304	
Mild Impairment	123	73 (59.3)	50 (40.7)	4.9 (3.7, 7.2)	69	36 (52.2)	33 (47.8)	4.2 (2.7, 7.9)	0.8257 (0.5502, 1.2391) 0.3551	0.3542	
Moderate Impairment	41	20 (48.8)	21 (51.2)	7.0 (1.6, NE)	23	11 (47.8)	12 (52.2)	11.1 (1.5, NE)	0.9703 (0.4608, 2.0431) 0.9368	0.9324	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.5935
Normal Function	170	98 (57.6)	72 (42.4)	5.6 (4.1, 8.3)	98	54 (55.1)	44 (44.9)	5.8 (3.3, 7.9)	0.8295 (0.5924, 1.1615)	0.2617	
Mild Impairment	195	106 (54.4)	89 (45.6)	7.0 (4.4, 8.8)	84	43 (51.2)	41 (48.8)	3.9 (2.3, 5.7)	0.7084 (0.4936, 1.0168)	0.0597	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.8475
Yes	332	181 (54.5)	151 (45.5)	6.9 (5.0, 8.1)	157	82 (52.2)	75 (47.8)	4.3 (3.1, 6.9)	0.7663 (0.5882, 0.9982) 0.0485	0.0461	
No	41	24 (58.5)	17 (41.5)	4.2 (1.4, NE)	27	15 (55.6)	12 (44.4)	4.4 (1.5, 9.0)	0.9331 (0.4859, 1.7920) 0.8353	0.8174	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.4973
Positive	331	179 (54.1)	152 (45.9)	6.9 (5.0, 9.7)	163	84 (51.5)	79 (48.5)	4.3 (3.2, 7.0)	0.7655 (0.5887, 0.9954) 0.0461	0.0434	
Negative	42	26 (61.9)	16 (38.1)	3.1 (1.8, 7.6)	21	13 (61.9)	8 (38.1)	5.3 (1.5, 6.9)	0.9441 (0.4794, 1.8591) 0.8678	0.8556	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.3960
Positive	333	181 (54.4)	152 (45.6)	6.9 (4.4, 8.4)	166	88 (53.0)	78 (47.0)	4.2 (3.2, 6.3)	0.7596 (0.5867, 0.9835) 0.0370	0.0343	
Negative	40	24 (60.0)	16 (40.0)	4.7 (2.8, 7.7)	18	9 (50.0)	9 (50.0)	5.9 (1.5, 9.0)	0.9927 (0.4566, 2.1584) 0.9853	0.9772	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.4378
HER2 IHC 1+	214	126 (58.9)	88 (41.1)	4.3 (3.0, 8.2)	107	66 (61.7)	41 (38.3)	2.8 (1.5, 4.4)	0.6598 (0.4863, 0.8951)	0.0073
HER2 IHC 2+/ISH Negative	159	85 (53.5)	74 (46.5)	9.7 (4.3, 12.5)	77	41 (53.2)	36 (46.8)	4.4 (3.1, 6.2)	0.7918 (0.5435, 1.1535)	0.2168

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.0970
1	221	135 (61.1)	86 (38.9)	4.2 (3.0, 5.9)	100	57 (57.0)	43 (43.0)	4.2 (1.5, 6.0)	0.8542 (0.6254, 1.1667) 0.3218	0.3282	
>=2	151	76 (50.3)	75 (49.7)	10.8 (5.6, 13.6)	83	50 (60.2)	33 (39.8)	3.4 (2.1, 5.4)	0.5532 (0.3823, 0.8003) 0.0017	0.0013	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.7276
Yes	235	132 (56.2)	103 (43.8)	5.6 (4.2, 8.5)	118	70 (59.3)	48 (40.7)	2.8 (1.9, 4.4)	0.6941 (0.5176, 0.9307) 0.0147	0.0140	
No	98	60 (61.2)	38 (38.8)	5.9 (3.5, 12.8)	48	27 (56.3)	21 (43.8)	5.4 (1.5, 7.9)	0.7634 (0.4800, 1.2143) 0.2543	0.2526	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0930
<65	290	162 (55.9)	128 (44.1)	7.0 (4.2, 10.0)	136	80 (58.8)	56 (41.2)	2.8 (1.7, 4.3)	0.6451 (0.4915, 0.8465) 0.0016	0.0014	
>=65	83	49 (59.0)	34 (41.0)	5.6 (3.1, 10.8)	48	27 (56.3)	21 (43.8)	6.5 (3.1, 8.6)	0.9228 (0.5680, 1.4994) 0.7457	0.7369	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0605
<75	359	202 (56.3)	157 (43.7)	5.9 (4.2, 9.7)	175	103 (58.9)	72 (41.1)	3.2 (2.0, 4.4)	0.6748 (0.5300, 0.8591) 0.0014	0.0013	
>=75	14	9 (64.3)	5 (35.7)	6.3 (0.9, 13.3)	9	4 (44.4)	5 (55.6)	11.3 (3.1, NE)	1.9407 (0.5918, 6.3643) 0.2739	0.2654	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.8897
White	176	100 (56.8)	76 (43.2)	4.3 (2.8, 10.0)	91	53 (58.2)	38 (41.8)	3.1 (1.8, 4.4)	0.7311 (0.5213, 1.0255) 0.0697	0.0677	
Non-White	197	111 (56.3)	86 (43.7)	7.0 (4.2, 11.3)	92	54 (58.7)	38 (41.3)	4.4 (1.9, 5.9)	0.6942 (0.4988, 0.9661) 0.0304	0.0286	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.6284
Asia	147	91 (61.9)	56 (38.1)	6.7 (4.2, 11.3)	66	42 (63.6)	24 (36.4)	4.2 (1.5, 6.0)	0.6828 (0.4713, 0.9893) 0.0437	0.0419	
North America	60	28 (46.7)	32 (53.3)	5.8 (2.8, 11.2)	33	19 (57.6)	14 (42.4)	2.1 (1.4, 4.7)	0.5933 (0.3275, 1.0750) 0.0852	0.0809	
Europe + Israel	166	92 (55.4)	74 (44.6)	5.6 (3.1, 10.3)	85	46 (54.1)	39 (45.9)	4.2 (2.7, 6.5)	0.8027 (0.5602, 1.1501) 0.2311	0.2256	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.0236
0	200	111 (55.5)	89 (44.5)	8.2 (4.3, 11.1)	105	64 (61.0)	41 (39.0)	2.7 (1.5, 4.2)	0.5583 (0.4080, 0.7639) 0.0003	0.0002	
1	173	100 (57.8)	73 (42.2)	4.2 (2.8, 9.7)	79	43 (54.4)	36 (45.6)	5.4 (3.4, 6.9)	0.9435 (0.6561, 1.3569) 0.7538	0.7359	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.3401
0	60	35 (58.3)	25 (41.7)	3.4 (1.7, 12.5)	34	20 (58.8)	14 (41.2)	4.2 (1.0, 5.9)	0.7150 (0.4069, 1.2565) 0.2436	0.2410	
1	108	59 (54.6)	49 (45.4)	4.2 (2.9, 12.4)	51	30 (58.8)	21 (41.2)	4.4 (1.5, 7.9)	0.7679 (0.4933, 1.1952) 0.2420	0.2397	
2	115	60 (52.2)	55 (47.8)	7.7 (4.4, 12.7)	54	33 (61.1)	21 (38.9)	2.7 (1.5, 5.4)	0.5282 (0.3401, 0.8203) 0.0045	0.0038	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	57 (63.3)	33 (36.7)	6.7 (4.1, 9.7)	45	24 (53.3)	21 (46.7)	4.2 (1.8, 6.2)	0.9223 (0.5683, 1.4969) 0.7435	0.7379

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.3033
PD	174	90 (51.7)	84 (48.3)	5.9 (3.1, 10.8)	85	45 (52.9)	40 (47.1)	4.3 (2.8, 5.8)	0.7719 (0.5341, 1.1156) 0.1682	0.1590	
PR	48	34 (70.8)	14 (29.2)	4.2 (2.8, 7.6)	22	11 (50.0)	11 (50.0)	2.4 (1.0, NE)	0.9186 (0.4620, 1.8264) 0.8087	0.8122	
SD	82	43 (52.4)	39 (47.6)	9.7 (4.3, 21.7)	55	37 (67.3)	18 (32.7)	3.8 (1.4, 6.0)	0.5273 (0.3367, 0.8261) 0.0052	0.0048	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.0979
Yes	37	23 (62.2)	14 (37.8)	3.0 (1.4, 18.1)	15	5 (33.3)	10 (66.7)	6.0 (0.9, NE)	1.5214 (0.5742, 4.0310) 0.3986	0.4054	
No	336	188 (56.0)	148 (44.0)	6.7 (4.2, 9.7)	169	102 (60.4)	67 (39.6)	3.5 (2.1, 4.6)	0.6653 (0.5206, 0.8503) 0.0011	0.0010	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0208
Yes	24	16 (66.7)	8 (33.3)	3.0 (0.8, NE)	8	2 (25.0)	6 (75.0)	NE (0.8, NE)	2.6839 (0.6113, 11.7840) 0.1909	0.1746	
No	349	195 (55.9)	154 (44.1)	5.9 (4.2, 9.7)	176	105 (59.7)	71 (40.3)	3.4 (2.1, 4.4)	0.6655 (0.5228, 0.8473) 0.0009	0.0008	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0970
Normal Function	202	115 (56.9)	87 (43.1)	5.6 (3.9, 10.0)	87	52 (59.8)	35 (40.2)	3.4 (1.5, 4.4)	0.6576 (0.4717, 0.9168) 0.0134	0.0125	
Mild Impairment	123	70 (56.9)	53 (43.1)	7.0 (3.4, 12.4)	69	41 (59.4)	28 (40.6)	2.8 (1.5, 4.4)	0.6031 (0.4042, 0.9001) 0.0133	0.0123	
Moderate Impairment	41	24 (58.5)	17 (41.5)	5.6 (1.6, 13.6)	23	11 (47.8)	12 (52.2)	8.6 (5.9, NE)	1.4021 (0.6836, 2.8757) 0.3565	0.3561	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.5918
Normal Function	170	97 (57.1)	73 (42.9)	5.6 (3.5, 12.4)	98	55 (56.1)	43 (43.9)	4.4 (2.3, 6.0)	0.7782 (0.5567, 1.0877) 0.1421	0.1379	
Mild Impairment	195	113 (57.9)	82 (42.1)	5.9 (4.2, 9.1)	84	51 (60.7)	33 (39.3)	2.9 (1.7, 4.3)	0.6478 (0.4620, 0.9084) 0.0118	0.0112	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.2900
Yes	332	187 (56.3)	145 (43.7)	5.9 (4.2, 9.7)	157	88 (56.1)	69 (43.9)	4.2 (2.8, 5.4)	0.7422 (0.5742, 0.9593) 0.0228	0.0221	
No	41	24 (58.5)	17 (41.5)	5.6 (1.4, NE)	27	19 (70.4)	8 (29.6)	1.5 (1.0, 4.6)	0.6079 (0.3257, 1.1348) 0.1181	0.1104	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.7891
Positive	331	189 (57.1)	142 (42.9)	5.9 (4.2, 9.7)	163	93 (57.1)	70 (42.9)	4.2 (2.3, 5.4)	0.7188 (0.5588, 0.9246) 0.0102	0.0098	
Negative	42	22 (52.4)	20 (47.6)	5.6 (1.4, NE)	21	14 (66.7)	7 (33.3)	3.4 (1.4, 5.9)	0.6953 (0.3481, 1.3889) 0.3033	0.2922	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.9836
Positive	333	191 (57.4)	142 (42.6)	5.9 (4.2, 9.7)	166	97 (58.4)	69 (41.6)	3.8 (2.1, 4.7)	0.7127 (0.5562, 0.9132) 0.0074	0.0070	
Negative	40	20 (50.0)	20 (50.0)	7.0 (1.6, NE)	18	10 (55.6)	8 (44.4)	4.2 (1.5, 7.0)	0.7162 (0.3276, 1.5658) 0.4030	0.3941	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.4160
HER2 IHC 1+	214	138 (64.5)	76 (35.5)	4.2 (2.5, 5.6)	107	63 (58.9)	44 (41.1)	1.5 (1.4, 2.9)	0.7274 (0.5371, 0.9851) 0.0397	0.0410	
HER2 IHC 2+/ISH Negative	159	102 (64.2)	57 (35.8)	4.2 (2.8, 5.6)	77	48 (62.3)	29 (37.7)	3.0 (1.4, 5.9)	0.8696 (0.6164, 1.2269) 0.4263	0.4135	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.2902
1	221	148 (67.0)	73 (33.0)	3.0 (1.7, 4.9)	100	66 (66.0)	34 (34.0)	1.5 (1.0, 2.8)	0.7071 (0.5275, 0.9479) 0.0204	0.0204
>=2	151	91 (60.3)	60 (39.7)	4.3 (2.8, 5.7)	83	45 (54.2)	38 (45.8)	3.2 (1.6, 6.1)	0.8852 (0.6178, 1.2686) 0.5067	0.5030

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.1041
Yes	235	157 (66.8)	78 (33.2)	3.0 (2.0, 4.2)	118	68 (57.6)	50 (42.4)	1.9 (1.4, 3.3)	0.8879 (0.6666, 1.1825) 0.4159	0.4133	
No	98	60 (61.2)	38 (38.8)	5.7 (4.2, 11.8)	48	33 (68.8)	15 (31.3)	2.9 (1.2, 6.1)	0.5377 (0.3478, 0.8311) 0.0052	0.0050	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1270
<65	290	177 (61.0)	113 (39.0)	4.4 (3.0, 5.8)	136	78 (57.4)	58 (42.6)	2.7 (1.4, 3.3)	0.7279 (0.5556, 0.9535) 0.0212	0.0206	
>=65	83	63 (75.9)	20 (24.1)	1.7 (1.4, 4.2)	48	33 (68.8)	15 (31.3)	1.9 (1.0, 4.5)	1.0649 (0.6978, 1.6251) 0.7707	0.7770	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2496
<75	359	230 (64.1)	129 (35.9)	4.2 (2.8, 5.5)	175	105 (60.0)	70 (40.0)	2.3 (1.4, 3.1)	0.7594 (0.6014, 0.9591) 0.0208	0.0206	
>=75	14	10 (71.4)	4 (28.6)	2.1 (0.8, 4.2)	9	6 (66.7)	3 (33.3)	3.1 (0.7, NE)	1.3050 (0.4729, 3.6013) 0.6073	0.5991	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.1355
White	176	117 (66.5)	59 (33.5)	3.0 (1.6, 4.2)	91	52 (57.1)	39 (42.9)	2.9 (1.4, 4.2)	0.9406 (0.6773, 1.3063) 0.7147	0.7046	
Non-White	197	123 (62.4)	74 (37.6)	4.7 (2.9, 5.8)	92	59 (64.1)	33 (35.9)	1.6 (1.3, 3.1)	0.6714 (0.4903, 0.9194) 0.0130	0.0130	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.1517
Asia	147	96 (65.3)	51 (34.7)	4.9 (2.9, 7.2)	66	44 (66.7)	22 (33.3)	1.5 (1.0, 3.1)	0.6409 (0.4465, 0.9198) 0.0158	0.0164	
North America	60	34 (56.7)	26 (43.3)	4.2 (3.0, 5.8)	33	18 (54.5)	15 (45.5)	2.0 (1.0, 4.5)	0.6020 (0.3356, 1.0799) 0.0887	0.0856	
Europe + Israel	166	110 (66.3)	56 (33.7)	2.8 (1.5, 4.2)	85	49 (57.6)	36 (42.4)	3.0 (1.4, 5.3)	1.0307 (0.7348, 1.4455) 0.8611	0.8708	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
ECOG PS											0.7579
0	200	140 (70.0)	60 (30.0)	4.2 (2.2, 5.5)	105	62 (59.0)	43 (41.0)	1.5 (1.3, 4.2)	0.8152 (0.6034, 1.1014) 0.1832	0.1921	
1	173	100 (57.8)	73 (42.2)	4.2 (2.8, 5.8)	79	49 (62.0)	30 (38.0)	2.9 (1.4, 4.0)	0.7565 (0.5350, 1.0697) 0.1144	0.1093	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.8507
0	60	36 (60.0)	24 (40.0)	5.3 (2.8, 9.7)	34	18 (52.9)	16 (47.1)	1.5 (0.8, 5.3)	0.6017 (0.3350, 1.0808) 0.0891	0.0905
1	108	67 (62.0)	41 (38.0)	4.2 (1.5, 5.7)	51	33 (64.7)	18 (35.3)	1.4 (0.9, 4.2)	0.7649 (0.5037, 1.1614) 0.2085	0.2141
2	115	74 (64.3)	41 (35.7)	4.2 (2.0, 5.7)	54	32 (59.3)	22 (40.7)	3.2 (1.5, 5.9)	0.8507 (0.5578, 1.2974) 0.4528	0.4245

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	63 (70.0)	27 (30.0)	3.6 (1.4, 4.6)	45	28 (62.2)	17 (37.8)	1.6 (0.9, 3.1)	0.8267 (0.5271, 1.2965) 0.4071	0.4087	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.8815
PD	174	102 (58.6)	72 (41.4)	4.2 (2.9, 6.1)	85	48 (56.5)	37 (43.5)	1.9 (1.4, 5.3)	0.7348 (0.5195, 1.0393)	0.0800
PR	48	31 (64.6)	17 (35.4)	3.2 (1.4, 11.2)	22	11 (50.0)	11 (50.0)	3.1 (0.8, NE)	0.8863 (0.4415, 1.7795)	0.7414
SD	82	59 (72.0)	23 (28.0)	4.3 (2.2, 5.6)	55	39 (70.9)	16 (29.1)	1.4 (1.0, 2.9)	0.6669 (0.4420, 1.0062)	0.0527

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.3693
Yes	37	23 (62.2)	14 (37.8)	4.2 (1.6, NE)	15	5 (33.3)	10 (66.7)	NE (0.8, NE)	1.2444 (0.4672, 3.3143) 0.6618	0.6571	
No	336	217 (64.6)	119 (35.4)	4.2 (2.8, 4.9)	169	106 (62.7)	63 (37.3)	2.3 (1.4, 3.1)	0.7693 (0.6083, 0.9727) 0.0285	0.0278	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.1412
Yes	24	14 (58.3)	10 (41.7)	4.9 (1.4, NE)	8	2 (25.0)	6 (75.0)	NE (0.7, NE)	2.2696 (0.5071, 10.1577)	0.2667
No	349	226 (64.8)	123 (35.2)	4.2 (2.8, 4.7)	176	109 (61.9)	67 (38.1)	2.0 (1.4, 3.0)	0.7626 (0.6053, 0.9606)	0.0210

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.6285
Normal Function	202	124 (61.4)	78 (38.6)	4.3 (2.9, 5.7)	87	48 (55.2)	39 (44.8)	1.9 (1.2, 4.9)	0.7249 (0.5164, 1.0174) 0.0629	0.0612	
Mild Impairment	123	84 (68.3)	39 (31.7)	2.8 (1.4, 4.6)	69	44 (63.8)	25 (36.2)	2.7 (1.4, 3.2)	0.8601 (0.5938, 1.2459) 0.4255	0.4181	
Moderate Impairment	41	28 (68.3)	13 (31.7)	4.2 (1.7, 9.1)	23	15 (65.2)	8 (34.8)	4.5 (0.8, 12.3)	0.9789 (0.5222, 1.8352) 0.9470	0.9637	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.5419
Normal Function	170	117 (68.8)	53 (31.2)	4.2 (2.0, 5.7)	98	63 (64.3)	35 (35.7)	1.5 (1.1, 4.0)	0.7484 (0.5494, 1.0194) 0.0661	0.0649	
Mild Impairment	195	121 (62.1)	74 (37.9)	4.2 (2.8, 4.7)	84	46 (54.8)	38 (45.2)	3.0 (1.4, 4.2)	0.8543 (0.6060, 1.2044) 0.3688	0.3693	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1888
Yes	332	215 (64.8)	117 (35.2)	4.2 (2.8, 4.4)	157	93 (59.2)	64 (40.8)	2.7 (1.4, 3.3)	0.8290 (0.6490, 1.0590) 0.1332	0.1350	
No	41	25 (61.0)	16 (39.0)	5.8 (1.0, 14.5)	27	18 (66.7)	9 (33.3)	1.5 (0.8, 4.5)	0.5547 (0.2947, 1.0440) 0.0678	0.0582	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.5887
Positive	331	216 (65.3)	115 (34.7)	4.2 (2.8, 4.9)	163	97 (59.5)	66 (40.5)	2.7 (1.4, 3.3)	0.8004 (0.6287, 1.0189) 0.0707	0.0712	
Negative	42	24 (57.1)	18 (42.9)	2.9 (1.4, 17.6)	21	14 (66.7)	7 (33.3)	1.4 (0.8, 5.3)	0.7088 (0.3625, 1.3858) 0.3143	0.3079	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.6945
Positive	333	216 (64.9)	117 (35.1)	4.2 (2.8, 5.3)	166	101 (60.8)	65 (39.2)	2.3 (1.4, 3.1)	0.7717 (0.6081, 0.9793) 0.0330	0.0329	
Negative	40	24 (60.0)	16 (40.0)	2.8 (1.4, 8.4)	18	10 (55.6)	8 (44.4)	1.5 (0.8, NE)	0.9405 (0.4455, 1.9856) 0.8723	0.8721	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0456
HER2 IHC 1+	214	156 (72.9)	58 (27.1)	1.4 (1.4, 1.7)	107	38 (35.5)	69 (64.5)	8.6 (6.0, NE)	2.6228 (1.8362, 3.7466) <0.0001	<0.0001	
HER2 IHC 2+/ISH Negative	159	102 (64.2)	57 (35.8)	1.6 (1.4, 2.8)	77	35 (45.5)	42 (54.5)	6.7 (4.6, 13.3)	1.5382 (1.0462, 2.2615) 0.0285	0.0290	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.9838
1	221	154 (69.7)	67 (30.3)	1.4 (1.4, 1.8)	100	42 (42.0)	58 (58.0)	7.0 (5.9, 11.3)	2.0363 (1.4444, 2.8707) <0.0001	<0.0001	
>=2	151	103 (68.2)	48 (31.8)	1.6 (1.4, 2.9)	83	31 (37.3)	52 (62.7)	8.6 (5.4, NE)	2.0619 (1.3777, 3.0860) 0.0004	0.0004	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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## Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.7770
Yes	235	164 (69.8)	71 (30.2)	1.6 (1.4, 2.4)	118	45 (38.1)	73 (61.9)	6.7 (5.4, 13.3)	2.1248 (1.5259, 2.9587) <0.0001	<0.0001	
No	98	69 (70.4)	29 (29.6)	1.4 (0.9, 2.8)	48	22 (45.8)	26 (54.2)	8.6 (4.2, 14.8)	1.8209 (1.1233, 2.9515) 0.0150	0.0152	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6782
<65	290	204 (70.3)	86 (29.7)	1.4 (1.4, 1.8)	136	52 (38.2)	84 (61.8)	8.6 (5.9, 13.3)	2.1338 (1.5716, 2.8970) <0.0001	<0.0001	
>=65	83	54 (65.1)	29 (34.9)	1.6 (1.4, 2.8)	48	21 (43.8)	27 (56.3)	7.5 (4.6, NE)	1.8782 (1.1294, 3.1236) 0.0152	0.0141	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3547
<75	359	247 (68.8)	112 (31.2)	1.5 (1.4, 1.8)	175	69 (39.4)	106 (60.6)	7.5 (5.9, 9.8)	2.0140 (1.5403, 2.6334) <0.0001	<0.0001	
>=75	14	11 (78.6)	3 (21.4)	1.4 (0.9, 2.8)	9	4 (44.4)	5 (55.6)	11.3 (0.7, NE)	5.3742 (1.4186, 20.3597) 0.0133	0.0069	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.3873
White	176	126 (71.6)	50 (28.4)	1.4 (1.4, 1.6)	91	33 (36.3)	58 (63.7)	8.2 (5.1, NE)	2.3899 (1.6265, 3.5115) <0.0001	<0.0001	
Non-White	197	132 (67.0)	65 (33.0)	1.6 (1.4, 2.8)	92	40 (43.5)	52 (56.5)	8.6 (5.9, 11.3)	1.8005 (1.2611, 2.5707) 0.0012	0.0011	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.4643
Asia	147	100 (68.0)	47 (32.0)	1.7 (1.4, 3.0)	66	30 (45.5)	36 (54.5)	8.6 (4.7, NE)	1.6366 (1.0856, 2.4674) 0.0187	0.0186	
North America	60	40 (66.7)	20 (33.3)	1.4 (0.9, 2.4)	33	9 (27.3)	24 (72.7)	6.3 (5.9, NE)	2.5724 (1.2440, 5.3194) 0.0108	0.0084	
Europe + Israel	166	118 (71.1)	48 (28.9)	1.4 (1.4, 1.6)	85	34 (40.0)	51 (60.0)	7.0 (4.6, 9.8)	2.4090 (1.6409, 3.5366) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											
0	200	139 (69.5)	61 (30.5)	1.4 (1.4, 2.4)	105	41 (39.0)	64 (61.0)	7.0 (5.1, 14.8)	1.9519 (1.3751, 2.7707) 0.0002	0.0001	0.5676
1	173	119 (68.8)	54 (31.2)	1.5 (1.4, 2.1)	79	32 (40.5)	47 (59.5)	8.6 (5.9, NE)	2.2256 (1.5033, 3.2949) 0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.9264
0	60	39 (65.0)	21 (35.0)	1.4 (1.0, 2.9)	34	11 (32.4)	23 (67.6)	9.0 (5.9, NE)	2.1593 (1.1027, 4.2285)	0.0213
1	108	67 (62.0)	41 (38.0)	1.8 (1.4, 2.9)	51	20 (39.2)	31 (60.8)	9.0 (4.7, NE)	2.0310 (1.2298, 3.3542)	0.0047
2	115	84 (73.0)	31 (27.0)	1.5 (1.4, 2.8)	54	21 (38.9)	33 (61.1)	6.3 (4.6, NE)	2.3686 (1.4658, 3.8274)	0.0003

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	68 (75.6)	22 (24.4)	1.4 (1.0, 1.7)	45	21 (46.7)	24 (53.3)	5.6 (1.5, NE)	1.8551 (1.1339, 3.0350) 0.0139	0.0138

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.8851
PD	174	113 (64.9)	61 (35.1)	1.5 (1.4, 2.8)	85	32 (37.6)	53 (62.4)	7.0 (5.1, 9.8)	2.0291 (1.3682, 3.0092) 0.0004	0.0003	
PR	48	36 (75.0)	12 (25.0)	1.4 (0.9, 1.6)	22	9 (40.9)	13 (59.1)	8.6 (1.7, NE)	2.4341 (1.1673, 5.0757) 0.0177	0.0154	
SD	82	57 (69.5)	25 (30.5)	1.6 (1.4, 3.2)	55	23 (41.8)	32 (58.2)	9.0 (4.7, NE)	1.8542 (1.1385, 3.0197) 0.0131	0.0120	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.7574
Yes	37	26 (70.3)	11 (29.7)	1.4 (0.9, 2.9)	15	4 (26.7)	11 (73.3)	NE (1.0, NE)	2.5730 (0.8970, 7.3811) 0.0788	0.0672	
No	336	232 (69.0)	104 (31.0)	1.5 (1.4, 1.8)	169	69 (40.8)	100 (59.2)	8.2 (5.9, 9.8)	2.0380 (1.5554, 2.6702) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.6107
Yes	24	16 (66.7)	8 (33.3)	1.4 (0.9, 13.0)	8	2 (25.0)	6 (75.0)	NE (0.8, NE)	2.8754 (0.6549, 12.6247)	0.1407
No	349	242 (69.3)	107 (30.7)	1.5 (1.4, 1.8)	176	71 (40.3)	105 (59.7)	8.2 (5.9, 9.8)	2.0485 (1.5704, 2.6723)	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.9363
Normal Function	202	140 (69.3)	62 (30.7)	1.6 (1.4, 2.8)	87	34 (39.1)	53 (60.9)	8.6 (5.1, NE)	1.9768 (1.3570, 2.8797) 0.0004	0.0003	
Mild Impairment	123	89 (72.4)	34 (27.6)	1.4 (1.4, 1.6)	69	28 (40.6)	41 (59.4)	7.5 (4.2, 9.8)	2.1841 (1.4234, 3.3512) 0.0003	0.0003	
Moderate Impairment	41	26 (63.4)	15 (36.6)	2.1 (1.0, 4.2)	23	10 (43.5)	13 (56.5)	8.2 (5.9, NE)	2.0099 (0.9627, 4.1961) 0.0631	0.0586	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.5304
Normal Function	170	133 (78.2)	37 (21.8)	1.4 (1.0, 1.4)	98	44 (44.9)	54 (55.1)	7.5 (5.4, 9.0)	2.2349 (1.5854, 3.1504) <0.0001	<0.0001
Mild Impairment	195	122 (62.6)	73 (37.4)	2.2 (1.5, 2.9)	84	29 (34.5)	55 (65.5)	9.8 (5.1, 13.3)	1.9638 (1.3082, 2.9480) 0.0011	0.0009

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Baseline visceral disease											
Yes	332	227 (68.4)	105 (31.6)	1.5 (1.4, 2.2)	157	58 (36.9)	99 (63.1)	8.6 (6.3, 13.3)	2.2026 (1.6487, 2.9427) <0.0001	<0.0001	0.4064
No	41	31 (75.6)	10 (24.4)	1.4 (0.9, 1.8)	27	15 (55.6)	12 (44.4)	5.9 (1.2, 9.0)	1.6103 (0.8622, 3.0073) 0.1350	0.1372	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (IXRS)										0.8140
Positive	331	232 (70.1)	99 (29.9)	1.5 (1.4, 1.8)	163	65 (39.9)	98 (60.1)	8.2 (5.9, 11.3)	2.0891 (1.5846, 2.7543) <0.0001	<0.0001
Negative	42	26 (61.9)	16 (38.1)	1.6 (1.0, 4.2)	21	8 (38.1)	13 (61.9)	9.0 (1.0, NE)	1.8598 (0.8372, 4.1315) 0.1276	0.1185

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.4896
Positive	333	231 (69.4)	102 (30.6)	1.5 (1.4, 2.1)	166	67 (40.4)	99 (59.6)	7.5 (5.9, 9.8)	2.0053 (1.5258, 2.6354) <0.0001	<0.0001	
Negative	40	27 (67.5)	13 (32.5)	1.4 (0.9, 2.8)	18	6 (33.3)	12 (66.7)	9.0 (1.5, NE)	2.7259 (1.1147, 6.6664) 0.0280	0.0227	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.8668
HER2 IHC 1+	214	113 (52.8)	101 (47.2)	9.6 (4.6, 11.8)	107	57 (53.3)	50 (46.7)	3.4 (2.1, 7.0)	0.5947 (0.4284, 0.8254) 0.0019	0.0017	
HER2 IHC 2+/ISH Negative	159	75 (47.2)	84 (52.8)	9.2 (6.9, 13.3)	77	40 (51.9)	37 (48.1)	4.7 (2.7, 7.2)	0.6404 (0.4336, 0.9459) 0.0251	0.0236	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.7777
1	221	118 (53.4)	103 (46.6)	8.5 (4.7, 11.1)	100	58 (58.0)	42 (42.0)	2.8 (1.5, 5.8)	0.5884 (0.4269, 0.8109) 0.0012	0.0010
>=2	151	69 (45.7)	82 (54.3)	10.6 (7.3, NE)	83	39 (47.0)	44 (53.0)	5.9 (3.4, 9.3)	0.6339 (0.4232, 0.9493) 0.0269	0.0253

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.3009
Yes	235	118 (50.2)	117 (49.8)	8.3 (4.6, 11.2)	118	60 (50.8)	58 (49.2)	4.4 (2.7, 7.3)	0.6654 (0.4850, 0.9128) 0.0116	0.0108	
No	98	54 (55.1)	44 (44.9)	9.7 (7.4, 13.4)	48	29 (60.4)	19 (39.6)	2.8 (1.4, 7.0)	0.5045 (0.3175, 0.8017) 0.0038	0.0032	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1237
<65	290	141 (48.6)	149 (51.4)	9.7 (7.7, 13.1)	136	72 (52.9)	64 (47.1)	4.0 (2.3, 5.8)	0.5588 (0.4181, 0.7469) 0.0001	<0.0001	
>=65	83	47 (56.6)	36 (43.4)	5.6 (2.8, 11.2)	48	25 (52.1)	23 (47.9)	7.0 (1.5, 8.3)	0.8560 (0.5204, 1.4081) 0.5403	0.5449	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7286
<75	359	183 (51.0)	176 (49.0)	9.2 (7.1, 11.1)	175	93 (53.1)	82 (46.9)	4.4 (2.4, 5.9)	0.6036 (0.4676, 0.7791) 0.0001	<0.0001	
>=75	14	5 (35.7)	9 (64.3)	NE (0.9, NE)	9	4 (44.4)	5 (55.6)	NE (0.7, NE)	0.9748 (0.2612, 3.6388) 0.9697	0.9698	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.8538
White	176	82 (46.6)	94 (53.4)	8.7 (5.8, 14.1)	91	44 (48.4)	47 (51.6)	4.0 (2.7, 7.7)	0.6134 (0.4226, 0.8903) 0.0101	0.0093	
Non-White	197	106 (53.8)	91 (46.2)	9.2 (5.4, 11.2)	92	52 (56.5)	40 (43.5)	4.6 (1.8, 6.1)	0.6330 (0.4506, 0.8892) 0.0084	0.0077	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Region											0.8691
Asia	147	84 (57.1)	63 (42.9)	9.6 (5.4, 12.7)	66	40 (60.6)	26 (39.4)	4.2 (1.5, 5.9)	0.5908 (0.4017, 0.8690) 0.0075	0.0067	
North America	60	22 (36.7)	38 (63.3)	10.6 (2.9, NE)	33	14 (42.4)	19 (57.6)	4.5 (1.5, 7.2)	0.6086 (0.3065, 1.2088) 0.1561	0.1471	
Europe + Israel	166	82 (49.4)	84 (50.6)	8.7 (5.7, 12.6)	85	43 (50.6)	42 (49.4)	4.4 (2.7, 7.7)	0.6599 (0.4537, 0.9598) 0.0297	0.0279	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.4115
0	200	110 (55.0)	90 (45.0)	8.7 (5.7, 11.8)	105	58 (55.2)	47 (44.8)	3.0 (1.5, 5.8)	0.5555 (0.4012, 0.7690) 0.0004	0.0003	
1	173	78 (45.1)	95 (54.9)	9.7 (5.9, 13.3)	79	39 (49.4)	40 (50.6)	5.8 (3.2, 9.8)	0.7126 (0.4814, 1.0546) 0.0902	0.0860	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.4163
0	60	31 (51.7)	29 (48.3)	7.7 (4.2, 17.6)	34	17 (50.0)	17 (50.0)	5.4 (1.4, 9.8)	0.6267 (0.3418, 1.1489) 0.1308	0.1271
1	108	53 (49.1)	55 (50.9)	8.8 (5.6, 13.5)	51	24 (47.1)	27 (52.9)	8.3 (3.1, 14.1)	0.8343 (0.5138, 1.3547) 0.4639	0.4624
2	115	57 (49.6)	58 (50.4)	10.5 (4.2, 13.3)	54	27 (50.0)	27 (50.0)	4.4 (2.1, 7.5)	0.6304 (0.3916, 1.0147) 0.0574	0.0527

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	47 (52.2)	43 (47.8)	10.2 (4.3, 13.4)	45	29 (64.4)	16 (35.6)	2.0 (1.4, 4.6)	0.4621 (0.2842, 0.7513) 0.0019	0.0014

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.7522
PD	174	80 (46.0)	94 (54.0)	9.6 (5.6, 12.7)	85	41 (48.2)	44 (51.8)	5.8 (2.7, 7.7)	0.6424 (0.4373, 0.9436) 0.0241	0.0229
PR	48	26 (54.2)	22 (45.8)	9.7 (4.2, 16.4)	22	9 (40.9)	13 (59.1)	7.0 (1.6, NE)	0.7993 (0.3662, 1.7445) 0.5737	0.5518
SD	82	46 (56.1)	36 (43.9)	9.7 (4.3, 14.1)	55	33 (60.0)	22 (40.0)	4.0 (1.5, 9.3)	0.5759 (0.3625, 0.9147) 0.0194	0.0187

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.2940
Yes	37	17 (45.9)	20 (54.1)	8.5 (5.4, NE)	15	4 (26.7)	11 (73.3)	NE (1.5, NE)	1.0651 (0.3523, 3.2206) 0.9110	0.9063
No	336	171 (50.9)	165 (49.1)	9.6 (6.9, 11.2)	169	93 (55.0)	76 (45.0)	4.4 (2.4, 5.8)	0.6000 (0.4633, 0.7771) 0.0001	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.1595
Yes	24	11 (45.8)	13 (54.2)	9.6 (5.4, NE)	8	2 (25.0)	6 (75.0)	NE (0.8, NE)	1.3891 (0.3033, 6.3614) 0.6721	0.6679	
No	349	177 (50.7)	172 (49.3)	9.2 (7.0, 11.2)	176	95 (54.0)	81 (46.0)	4.4 (2.4, 5.8)	0.5975 (0.4629, 0.7713) 0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.2410
Normal Function	202	98 (48.5)	104 (51.5)	10.2 (8.3, 12.7)	87	47 (54.0)	40 (46.0)	4.0 (2.0, 7.2)	0.5070 (0.3539, 0.7263) 0.0002	0.0002	
Mild Impairment	123	66 (53.7)	57 (46.3)	5.8 (3.0, 13.1)	69	36 (52.2)	33 (47.8)	4.4 (1.5, 7.0)	0.7147 (0.4722, 1.0818) 0.1123	0.1086	
Moderate Impairment	41	21 (51.2)	20 (48.8)	8.8 (4.2, 13.5)	23	11 (47.8)	12 (52.2)	7.3 (3.1, NE)	0.9779 (0.4699, 2.0351) 0.9523	0.9596	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.5553
Normal Function	170	95 (55.9)	75 (44.1)	8.5 (4.4, 11.1)	98	53 (54.1)	45 (45.9)	4.4 (2.7, 5.8)	0.7105 (0.5051, 0.9994) 0.0496	0.0463	
Mild Impairment	195	91 (46.7)	104 (53.3)	10.2 (7.1, 13.1)	84	42 (50.0)	42 (50.0)	7.2 (2.0, 8.7)	0.5689 (0.3908, 0.8282) 0.0032	0.0029	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline visceral disease										0.4947
Yes	332	164 (49.4)	168 (50.6)	9.7 (7.1, 12.5)	157	83 (52.9)	74 (47.1)	4.2 (2.4, 7.0)	0.6054 (0.4624, 0.7925) 0.0003	0.0002
No	41	24 (58.5)	17 (41.5)	7.7 (2.8, 12.6)	27	14 (51.9)	13 (48.1)	4.4 (1.5, NE)	0.7297 (0.3688, 1.4438) 0.3654	0.3557

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.9664
Positive	331	172 (52.0)	159 (48.0)	8.8 (7.0, 10.6)	163	87 (53.4)	76 (46.6)	4.2 (2.4, 6.1)	0.6103 (0.4691, 0.7939) 0.0002	0.0002	
Negative	42	16 (38.1)	26 (61.9)	17.6 (4.7, NE)	21	10 (47.6)	11 (52.4)	5.9 (1.4, NE)	0.7317 (0.3269, 1.6376) 0.4472	0.4383	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (derived)										0.5850
Positive	333	171 (51.4)	162 (48.6)	8.8 (7.1, 10.6)	166	89 (53.6)	77 (46.4)	4.2 (2.4, 6.1)	0.5991 (0.4613, 0.7782) 0.0001	0.0001
Negative	40	17 (42.5)	23 (57.5)	17.6 (1.6, NE)	18	8 (44.4)	10 (55.6)	5.9 (1.4, NE)	0.9099 (0.3875, 2.1365) 0.8284	0.8198

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.0926
HER2 IHC 1+	214	98 (45.8)	116 (54.2)	11.2 (7.1, 15.7)	107	37 (34.6)	70 (65.4)	NE (5.0, NE)	0.9281 (0.6329, 1.3610) 0.7025	0.7073
HER2 IHC 2+/ISH Negative	159	66 (41.5)	93 (58.5)	21.7 (8.1, NE)	77	37 (48.1)	40 (51.9)	6.5 (3.8, 9.4)	0.5811 (0.3847, 0.8779) 0.0099	0.0089

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.6882
1	221	102 (46.2)	119 (53.8)	11.3 (6.9, 20.9)	100	42 (42.0)	58 (58.0)	6.5 (4.5, NE)	0.8097 (0.5624, 1.1660)	0.2555
>=2	151	62 (41.1)	89 (58.9)	15.3 (8.3, NE)	83	32 (38.6)	51 (61.4)	7.5 (4.4, NE)	0.6692 (0.4330, 1.0341)	0.0688

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.7119
Yes	235	104 (44.3)	131 (55.7)	11.8 (8.1, 16.7)	118	45 (38.1)	73 (61.9)	6.7 (4.4, NE)	0.7797 (0.5448, 1.1158)	0.1736	0.1719
No	98	45 (45.9)	53 (54.1)	12.5 (5.9, NE)	48	21 (43.8)	27 (56.3)	7.5 (3.8, NE)	0.7235 (0.4293, 1.2192)	0.2242	0.2240

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6233
<65	290	128 (44.1)	162 (55.9)	12.5 (8.3, 20.9)	136	51 (37.5)	85 (62.5)	6.5 (5.1, NE)	0.7781 (0.5583, 1.0845) 0.1386	0.1368	
>=65	83	36 (43.4)	47 (56.6)	11.1 (5.6, NE)	48	23 (47.9)	25 (52.1)	6.7 (1.7, NE)	0.6958 (0.4114, 1.1767) 0.1761	0.1755	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1676
<75	359	156 (43.5)	203 (56.5)	12.5 (8.8, 21.7)	175	69 (39.4)	106 (60.6)	6.5 (5.0, NE)	0.7264 (0.5440, 0.9698) 0.0301	0.0296	
>=75	14	8 (57.1)	6 (42.9)	5.6 (0.9, NE)	9	5 (55.6)	4 (44.4)	13.7 (1.4, NE)	1.7052 (0.5499, 5.2878) 0.3554	0.3477	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Race										0.8034
White	176	70 (39.8)	106 (60.2)	15.7 (10.2, NE)	91	33 (36.3)	58 (63.7)	6.8 (4.5, NE)	0.7151 (0.4677, 1.0934)	0.1197
Non-White	197	94 (47.7)	103 (52.3)	9.3 (6.9, 27.2)	92	41 (44.6)	51 (55.4)	6.1 (4.4, NE)	0.7783 (0.5372, 1.1275)	0.1856

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.1704
Asia	147	73 (49.7)	74 (50.3)	9.3 (6.5, 27.2)	66	29 (43.9)	37 (56.1)	6.5 (4.7, NE)	0.8603 (0.5574, 1.3277) 0.4967	0.4977	
North America	60	22 (36.7)	38 (63.3)	13.2 (4.5, NE)	33	16 (48.5)	17 (51.5)	3.1 (1.4, 5.0)	0.4012 (0.2029, 0.7936) 0.0087	0.0071	
Europe + Israel	166	69 (41.6)	97 (58.4)	16.7 (8.8, NE)	85	29 (34.1)	56 (65.9)	7.5 (6.5, NE)	0.8495 (0.5457, 1.3225) 0.4701	0.4683	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	200	95 (47.5)	105 (52.5)	11.2 (7.5, 21.7)	105	39 (37.1)	66 (62.9)	6.7 (5.1, NE)	0.8403 (0.5749, 1.2283) 0.3690	0.3711	0.3791
1	173	69 (39.9)	104 (60.1)	15.3 (7.1, NE)	79	35 (44.3)	44 (55.7)	6.8 (3.8, NE)	0.6612 (0.4376, 0.9989) 0.0494	0.0473	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.3229
0	60	23 (38.3)	37 (61.7)	11.1 (5.8, NE)	34	14 (41.2)	20 (58.8)	5.8 (2.9, NE)	0.5632 (0.2861, 1.1085)	0.0942
1	108	47 (43.5)	61 (56.5)	15.7 (5.6, 24.1)	51	17 (33.3)	34 (66.7)	NE (4.2, NE)	1.0302 (0.5854, 1.8130)	0.9192
2	115	59 (51.3)	56 (48.7)	8.1 (5.7, 13.2)	54	24 (44.4)	30 (55.6)	6.7 (2.1, 9.7)	0.7680 (0.4726, 1.2480)	0.2823

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	35 (38.9)	55 (61.1)	NE (6.9, NE)	45	19 (42.2)	26 (57.8)	8.4 (1.6, NE)	0.5896 (0.3339, 1.0411) 0.0686	0.0664

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.6858
PD	174	72 (41.4)	102 (58.6)	15.3 (5.8, 27.2)	85	31 (36.5)	54 (63.5)	7.5 (5.1, NE)	0.8529 (0.5570, 1.3059) 0.4640	0.4633
PR	48	19 (39.6)	29 (60.4)	NE (10.2, NE)	22	9 (40.9)	13 (59.1)	6.7 (1.7, NE)	0.6235 (0.2757, 1.4102) 0.2566	0.2529
SD	82	32 (39.0)	50 (61.0)	NE (7.9, NE)	55	24 (43.6)	31 (56.4)	6.8 (3.1, NE)	0.6174 (0.3607, 1.0567) 0.0786	0.0755

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.3541
Yes	37	13 (35.1)	24 (64.9)	NE (4.5, NE)	15	5 (33.3)	10 (66.7)	NE (0.8, NE)	0.5289 (0.1833, 1.5263) 0.2388	0.2332	
No	336	151 (44.9)	185 (55.1)	11.8 (8.1, 16.7)	169	69 (40.8)	100 (59.2)	6.7 (5.1, 13.7)	0.7785 (0.5827, 1.0400) 0.0902	0.0894	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.5392
Yes	24	9 (37.5)	15 (62.5)	NE (4.4, NE)	8	3 (37.5)	5 (62.5)	NE (0.7, NE)	0.6218 (0.1625, 2.3797) 0.4878	0.4928	
No	349	155 (44.4)	194 (55.6)	11.8 (8.3, 20.9)	176	71 (40.3)	105 (59.7)	6.7 (5.1, 13.7)	0.7623 (0.5729, 1.0143) 0.0625	0.0617	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Renal function at baseline										0.8662
Normal Function	202	80 (39.6)	122 (60.4)	16.7 (10.2, NE)	87	30 (34.5)	57 (65.5)	8.4 (4.4, NE)	0.7708 (0.5028, 1.1817) 0.2324	0.2295
Mild Impairment	123	62 (50.4)	61 (49.6)	8.3 (5.6, 13.2)	69	27 (39.1)	42 (60.9)	6.5 (5.0, NE)	0.8395 (0.5279, 1.3348) 0.4596	0.4600
Moderate Impairment	41	19 (46.3)	22 (53.7)	9.1 (4.2, NE)	23	13 (56.5)	10 (43.5)	5.9 (1.5, NE)	0.7589 (0.3745, 1.5379) 0.4439	0.4410

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.5447
Normal Function	170	80 (47.1)	90 (52.9)	11.1 (7.1, NE)	98	43 (43.9)	55 (56.1)	6.7 (4.5, 13.7)	0.7311 (0.5023, 1.0642) 0.1021	0.1009
Mild Impairment	195	82 (42.1)	113 (57.9)	13.2 (7.1, 21.7)	84	29 (34.5)	55 (65.5)	9.7 (4.2, NE)	0.8476 (0.5508, 1.3043) 0.4521	0.4503

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.6952
Yes	332	145 (43.7)	187 (56.3)	12.5 (8.8, 20.9)	157	63 (40.1)	94 (59.9)	6.8 (5.0, NE)	0.7267 (0.5377, 0.9820) 0.0377	0.0373	
No	41	19 (46.3)	22 (53.7)	5.8 (3.1, NE)	27	11 (40.7)	16 (59.3)	6.7 (4.4, NE)	1.0000 (0.4749, 2.1057) 1.0000	0.9975	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.7712
Positive	331	146 (44.1)	185 (55.9)	12.5 (8.3, 20.9)	163	65 (39.9)	98 (60.1)	6.7 (5.0, NE)	0.7410 (0.5505, 0.9974) 0.0480	0.0476	
Negative	42	18 (42.9)	24 (57.1)	9.3 (3.3, NE)	21	9 (42.9)	12 (57.1)	5.9 (2.9, NE)	0.8882 (0.3930, 2.0076) 0.7758	0.7716	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.6841
Positive	333	149 (44.7)	184 (55.3)	12.5 (8.3, 20.9)	166	66 (39.8)	100 (60.2)	6.7 (5.0, NE)	0.7659 (0.5705, 1.0283) 0.0760	0.0754	
Negative	40	15 (37.5)	25 (62.5)	11.1 (4.6, NE)	18	8 (44.4)	10 (55.6)	5.9 (1.5, NE)	0.6588 (0.2739, 1.5843) 0.3512	0.3429	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.2878
HER2 IHC 1+	214	92 (43.0)	122 (57.0)	12.0 (7.8, 18.6)	107	47 (43.9)	60 (56.1)	5.8 (2.9, 10.2)	0.5967 (0.4153, 0.8572) 0.0052	0.0047
HER2 IHC 2+/ISH Negative	159	57 (35.8)	102 (64.2)	18.3 (11.1, NE)	77	38 (49.4)	39 (50.6)	5.3 (3.7, 10.0)	0.4178 (0.2738, 0.6375) 0.0001	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.3206
1	221	92 (41.6)	129 (58.4)	12.0 (8.3, NE)	100	46 (46.0)	54 (54.0)	5.4 (3.3, 12.0)	0.5892 (0.4108, 0.8451) 0.0040	0.0037
>=2	151	56 (37.1)	95 (62.9)	16.6 (11.1, NE)	83	39 (47.0)	44 (53.0)	5.3 (2.8, 7.0)	0.4097 (0.2665, 0.6297) <0.0001	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Prior CDK4/6											
Yes	235	89 (37.9)	146 (62.1)	16.1 (9.7, NE)	118	51 (43.2)	67 (56.8)	5.0 (3.2, 10.2)	0.5353 (0.3765, 0.7612) 0.0005	0.0004	0.7806
No	98	44 (44.9)	54 (55.1)	16.0 (9.6, NE)	48	26 (54.2)	22 (45.8)	5.4 (2.9, 7.0)	0.4407 (0.2654, 0.7316) 0.0015	0.0011	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Age										0.1702
<65	290	113 (39.0)	177 (61.0)	17.6 (10.1, NE)	136	64 (47.1)	72 (52.9)	5.0 (3.7, 6.1)	0.4592 (0.3345, 0.6303)	<0.0001
>=65	83	36 (43.4)	47 (56.6)	11.8 (7.1, 18.6)	48	21 (43.8)	27 (56.3)	6.5 (2.8, NE)	0.6909 (0.3960, 1.2054)	0.1893

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Age										0.0309
<75	359	140 (39.0)	219 (61.0)	16.1 (11.1, NE)	175	81 (46.3)	94 (53.7)	5.0 (3.8, 7.0)	0.4751 (0.3578, 0.6310)	<0.0001
>=75	14	9 (64.3)	5 (35.7)	4.2 (1.4, NE)	9	4 (44.4)	5 (55.6)	NE (0.7, NE)	1.7710 (0.5381, 5.8289)	0.3439

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Race										0.6442
White	176	74 (42.0)	102 (58.0)	11.1 (8.3, 18.3)	91	41 (45.1)	50 (54.9)	5.3 (2.8, 10.0)	0.5329 (0.3589, 0.7912) 0.0018	0.0015
Non-White	197	75 (38.1)	122 (61.9)	16.6 (11.7, NE)	92	44 (47.8)	48 (52.2)	5.4 (3.7, 12.0)	0.4892 (0.3338, 0.7170) 0.0002	0.0002

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Region										0.7389
Asia	147	59 (40.1)	88 (59.9)	NE (11.7, NE)	66	35 (53.0)	31 (47.0)	5.0 (2.9, 12.0)	0.4891 (0.3188, 0.7503) 0.0011	0.0008
North America	60	19 (31.7)	41 (68.3)	NE (4.4, NE)	33	10 (30.3)	23 (69.7)	NE (1.8, NE)	0.7441 (0.3442, 1.6086) 0.4523	0.4542
Europe + Israel	166	71 (42.8)	95 (57.2)	11.2 (8.3, 17.6)	85	40 (47.1)	45 (52.9)	5.9 (2.8, 10.0)	0.4752 (0.3165, 0.7134) 0.0003	0.0002

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	200	77 (38.5)	123 (61.5)	16.1 (11.1, NE)	105	52 (49.5)	53 (50.5)	5.3 (1.8, 6.5)	0.3814 (0.2649, 0.5492)	<0.0001	0.0210
1	173	72 (41.6)	101 (58.4)	16.0 (7.3, 18.3)	79	33 (41.8)	46 (58.2)	6.1 (4.2, NE)	0.7578 (0.4973, 1.1549)	0.1919	0.1970

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.8997
0	60	30 (50.0)	30 (50.0)	9.2 (5.9, 17.6)	34	17 (50.0)	17 (50.0)	5.3 (1.7, 5.9)	0.5302 (0.2857, 0.9838) 0.0442	0.0405
1	108	37 (34.3)	71 (65.7)	NE (9.3, NE)	51	24 (47.1)	27 (52.9)	6.5 (1.5, 10.2)	0.5279 (0.3141, 0.8871) 0.0159	0.0142
2	115	46 (40.0)	69 (60.0)	NE (7.3, NE)	54	23 (42.6)	31 (57.4)	4.5 (2.1, NE)	0.5721 (0.3422, 0.9565) 0.0332	0.0309

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	36 (40.0)	54 (60.0)	16.0 (11.2, NE)	45	21 (46.7)	24 (53.3)	4.2 (1.9, NE)	0.4086 (0.2302, 0.7254) 0.0022	0.0017

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.3450
PD	174	63 (36.2)	111 (63.8)	16.6 (9.6, NE)	85	37 (43.5)	48 (56.5)	4.7 (2.8, NE)	0.4621 (0.3034, 0.7040) 0.0003	0.0002
PR	48	18 (37.5)	30 (62.5)	16.1 (11.7, NE)	22	12 (54.5)	10 (45.5)	4.2 (1.0, 7.0)	0.3122 (0.1437, 0.6779) 0.0033	0.0018
SD	82	36 (43.9)	46 (56.1)	17.6 (8.7, NE)	55	27 (49.1)	28 (50.9)	6.1 (2.9, 10.2)	0.5806 (0.3450, 0.9773) 0.0407	0.0386

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.5417
Yes	37	16 (43.2)	21 (56.8)	11.1 (5.6, NE)	15	5 (33.3)	10 (66.7)	2.8 (0.9, NE)	0.6629 (0.2371, 1.8533)	0.4424
No	336	133 (39.6)	203 (60.4)	16.1 (11.1, NE)	169	80 (47.3)	89 (52.7)	5.4 (4.2, 7.0)	0.4987 (0.3744, 0.6643)	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.3807
Yes	24	8 (33.3)	16 (66.7)	NE (8.3, NE)	8	2 (25.0)	6 (75.0)	NE (1.4, NE)	0.8469 (0.1753, 4.0917) 0.8361	0.8416	
No	349	141 (40.4)	208 (59.6)	16.0 (10.1, 18.6)	176	83 (47.2)	93 (52.8)	5.3 (3.8, 6.5)	0.5042 (0.3810, 0.6671) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Renal function at baseline										0.2293
Normal Function	202	78 (38.6)	124 (61.4)	16.0 (10.6, NE)	87	42 (48.3)	45 (51.7)	4.3 (2.8, 5.9)	0.4192 (0.2835, 0.6200)	<0.0001
Mild Impairment	123	51 (41.5)	72 (58.5)	13.4 (9.0, NE)	69	30 (43.5)	39 (56.5)	6.1 (2.8, 10.2)	0.5537 (0.3454, 0.8878)	0.0126
Moderate Impairment	41	18 (43.9)	23 (56.1)	9.3 (4.3, NE)	23	10 (43.5)	13 (56.5)	NE (1.9, NE)	0.9517 (0.4382, 2.0669)	0.9040

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.8385
Normal Function	170	78 (45.9)	92 (54.1)	11.8 (8.7, 18.3)	98	49 (50.0)	49 (50.0)	5.0 (2.9, 6.1)	0.5255 (0.3635, 0.7597) 0.0006	0.0005
Mild Impairment	195	70 (35.9)	125 (64.1)	17.6 (11.1, NE)	84	34 (40.5)	50 (59.5)	7.1 (3.2, NE)	0.5416 (0.3554, 0.8254) 0.0043	0.0041

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.2308
Yes	332	131 (39.5)	201 (60.5)	16.0 (11.1, 18.6)	157	69 (43.9)	88 (56.1)	5.9 (4.2, 10.0)	0.5488 (0.4069, 0.7403) 0.0001	<0.0001	
No	41	18 (43.9)	23 (56.1)	11.7 (6.3, NE)	27	16 (59.3)	11 (40.7)	4.5 (1.2, 5.8)	0.3391 (0.1635, 0.7034) 0.0037	0.0025	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (IXRS)											0.8677
Positive	331	133 (40.2)	198 (59.8)	16.0 (10.6, NE)	163	74 (45.4)	89 (54.6)	5.8 (4.2, 7.1)	0.5153 (0.3847, 0.6904) <0.0001	<0.0001	
Negative	42	16 (38.1)	26 (61.9)	17.6 (3.1, NE)	21	11 (52.4)	10 (47.6)	4.7 (1.4, NE)	0.5395 (0.2438, 1.1938) 0.1278	0.1175	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (derived)										0.4827
Positive	333	131 (39.3)	202 (60.7)	16.0 (11.1, NE)	166	77 (46.4)	89 (53.6)	5.4 (3.8, 7.1)	0.4974 (0.3723, 0.6646) <0.0001	<0.0001
Negative	40	18 (45.0)	22 (55.0)	10.6 (4.3, NE)	18	8 (44.4)	10 (55.6)	5.3 (1.4, NE)	0.6967 (0.2940, 1.6510) 0.4116	0.4064

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
HER2 status										0.7755
HER2 IHC 1+	214	123 (57.5)	91 (42.5)	5.1 (2.9, 8.1)	107	46 (43.0)	61 (57.0)	6.5 (4.0, 11.3)	1.1361 (0.8068, 1.5999)	0.4811
HER2 IHC 2+/ISH Negative	159	92 (57.9)	67 (42.1)	5.5 (2.9, 8.5)	77	34 (44.2)	43 (55.8)	6.3 (5.0, 14.4)	1.2142 (0.8187, 1.8007)	0.3413

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.1026
1	221	134 (60.6)	87 (39.4)	4.2 (2.8, 5.7)	100	42 (42.0)	58 (58.0)	8.5 (4.6, NE)	1.4447 (1.0206, 2.0449) 0.0380	0.0386
>=2	151	81 (53.6)	70 (46.4)	7.4 (4.3, 11.8)	83	38 (45.8)	45 (54.2)	6.1 (3.8, 9.8)	0.8827 (0.5965, 1.3061) 0.5325	0.5200

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Prior CDK4/6											
Yes	235	135 (57.4)	100 (42.6)	4.5 (2.9, 7.7)	118	47 (39.8)	71 (60.2)	6.3 (4.4, NE)	1.2504 (0.8951, 1.7467) 0.1901	0.1948	0.3656
No	98	58 (59.2)	40 (40.8)	5.6 (3.1, 11.2)	48	26 (54.2)	22 (45.8)	7.5 (3.1, 11.3)	0.9589 (0.6027, 1.5255) 0.8593	0.8529	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Age											
<65	290	165 (56.9)	125 (43.1)	5.1 (3.2, 8.1)	136	56 (41.2)	80 (58.8)	6.2 (4.4, 9.8)	1.1771 (0.8676, 1.5970) 0.2950	0.3032	0.7723
>=65	83	50 (60.2)	33 (39.8)	5.6 (1.6, 8.5)	48	24 (50.0)	24 (50.0)	7.0 (4.2, 11.7)	1.2182 (0.7466, 1.9876) 0.4295	0.4376	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4244
<75	359	203 (56.5)	156 (43.5)	5.6 (4.2, 7.7)	175	73 (41.7)	102 (58.3)	7.0 (5.1, 9.8)	1.1724 (0.8956, 1.5346) 0.2470	0.2576	
>=75	14	12 (85.7)	2 (14.3)	2.1 (1.4, 4.2)	9	7 (77.8)	2 (22.2)	6.5 (0.7, NE)	2.4946 (0.9164, 6.7907) 0.0736	0.0659	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Race										0.4947
White	176	96 (54.5)	80 (45.5)	5.6 (2.9, 8.6)	91	38 (41.8)	53 (58.2)	5.1 (4.0, 9.0)	1.0710 (0.7324, 1.5661)	0.7325
Non-White	197	119 (60.4)	78 (39.6)	4.7 (2.9, 7.6)	92	42 (45.7)	50 (54.3)	8.5 (4.4, 11.7)	1.2453 (0.8745, 1.7732)	0.2308

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Region										0.5841
Asia	147	97 (66.0)	50 (34.0)	4.2 (2.8, 7.4)	66	31 (47.0)	35 (53.0)	8.5 (3.8, 14.4)	1.3526 (0.9015, 2.0295) 0.1446	0.1454
North America	60	27 (45.0)	33 (55.0)	5.6 (1.5, NE)	33	9 (27.3)	24 (72.7)	6.3 (1.5, NE)	1.3091 (0.6097, 2.8108) 0.4896	0.4920
Europe + Israel	166	91 (54.8)	75 (45.2)	6.1 (2.9, 10.6)	85	40 (47.1)	45 (52.9)	6.2 (4.2, 9.0)	1.0000 (0.6862, 1.4573) 1.0000	0.9846

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	200	114 (57.0)	86 (43.0)	7.0 (4.2, 11.2)	105	45 (42.9)	60 (57.1)	7.0 (4.1, 11.7)	1.0507 (0.7425, 1.4868) 0.7801	0.7926	0.3660
1	173	101 (58.4)	72 (41.6)	4.2 (2.3, 5.9)	79	35 (44.3)	44 (55.7)	6.3 (5.0, 11.3)	1.3619 (0.9251, 2.0049) 0.1175	0.1215	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.6765
0	60	31 (51.7)	29 (48.3)	5.6 (1.4, NE)	34	14 (41.2)	20 (58.8)	5.9 (1.3, NE)	1.0401 (0.5510, 1.9634) 0.9034	0.9204
1	108	61 (56.5)	47 (43.5)	5.5 (2.3, 10.6)	51	22 (43.1)	29 (56.9)	8.5 (6.1, NE)	1.3579 (0.8321, 2.2159) 0.2207	0.2219
2	115	64 (55.7)	51 (44.3)	7.0 (4.2, 11.2)	54	24 (44.4)	30 (55.6)	5.1 (3.9, NE)	0.9239 (0.5716, 1.4932) 0.7465	0.7317

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	59 (65.6)	31 (34.4)	4.2 (1.6, 7.7)	45	20 (44.4)	25 (55.6)	6.2 (2.1, NE)	1.3450 (0.8080, 2.2390) 0.2543	0.2562

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.6603
PD	174	94 (54.0)	80 (46.0)	6.9 (3.2, 10.2)	85	38 (44.7)	47 (55.3)	6.3 (3.4, 8.5)	0.9580 (0.6544, 1.4023) 0.8252	0.8145	
PR	48	32 (66.7)	16 (33.3)	2.8 (0.9, 6.2)	22	10 (45.5)	12 (54.5)	6.0 (1.4, NE)	1.3510 (0.6624, 2.7556) 0.4080	0.4308	
SD	82	46 (56.1)	36 (43.9)	5.6 (3.9, 12.0)	55	24 (43.6)	31 (56.4)	9.0 (4.2, NE)	1.2527 (0.7638, 2.0546) 0.3721	0.3765	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.9261
Yes	37	19 (51.4)	18 (48.6)	4.5 (1.5, NE)	15	4 (26.7)	11 (73.3)	NE (0.8, NE)	1.4097 (0.4784, 4.1543) 0.5334	0.5320	
No	336	196 (58.3)	140 (41.7)	5.5 (3.4, 7.2)	169	76 (45.0)	93 (55.0)	6.5 (5.0, 9.8)	1.1730 (0.8987, 1.5311) 0.2404	0.2499	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Baseline CNS metastases										0.1896
Yes	24	17 (70.8)	7 (29.2)	1.6 (0.9, 8.5)	8	2 (25.0)	6 (75.0)	NE (0.8, NE)	2.9730 (0.6853, 12.8973)	0.1260
No	349	198 (56.7)	151 (43.3)	5.6 (4.2, 7.7)	176	78 (44.3)	98 (55.7)	6.5 (5.0, 9.8)	1.1154 (0.8569, 1.4520)	0.4317

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.1574
Normal Function	202	115 (56.9)	87 (43.1)	5.6 (2.9, 8.5)	87	36 (41.4)	51 (58.6)	6.3 (3.2, NE)	1.1773 (0.8082, 1.7148) 0.3951	0.4072	
Mild Impairment	123	69 (56.1)	54 (43.9)	5.6 (2.8, 11.2)	69	32 (46.4)	37 (53.6)	6.0 (3.4, 9.8)	0.9813 (0.6398, 1.5051) 0.9310	0.9146	
Moderate Impairment	41	28 (68.3)	13 (31.7)	4.2 (1.5, 8.5)	23	9 (39.1)	14 (60.9)	11.3 (6.5, NE)	2.2992 (1.0799, 4.8954) 0.0308	0.0267	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.2170
Normal Function	170	115 (67.6)	55 (32.4)	2.9 (1.6, 5.6)	98	45 (45.9)	53 (54.1)	6.5 (4.0, 11.7)	1.4217 (1.0060, 2.0091) 0.0461	0.0481	
Mild Impairment	195	97 (49.7)	98 (50.3)	8.5 (4.3, 13.5)	84	33 (39.3)	51 (60.7)	6.2 (4.4, 11.3)	1.0115 (0.6784, 1.5082) 0.9551	0.9634	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline visceral disease										0.7098
Yes	332	189 (56.9)	143 (43.1)	5.6 (4.2, 8.1)	157	66 (42.0)	91 (58.0)	7.0 (5.0, 11.3)	1.1946 (0.9010, 1.5838) 0.2166	0.2269
No	41	26 (63.4)	15 (36.6)	2.8 (1.3, 5.1)	27	14 (51.9)	13 (48.1)	5.9 (0.9, NE)	1.1286 (0.5885, 2.1641) 0.7158	0.7158

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (IXRS)										0.8217
Positive	331	192 (58.0)	139 (42.0)	5.6 (3.9, 7.4)	163	71 (43.6)	92 (56.4)	7.0 (4.6, 10.5)	1.1556 (0.8789, 1.5195) 0.3004	0.3102
Negative	42	23 (54.8)	19 (45.2)	2.9 (1.0, 13.5)	21	9 (42.9)	12 (57.1)	6.0 (1.0, NE)	1.3445 (0.6168, 2.9306) 0.4565	0.4580

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (derived)										0.6709
Positive	333	193 (58.0)	140 (42.0)	5.5 (3.9, 7.2)	166	73 (44.0)	93 (56.0)	7.0 (4.6, 10.5)	1.1482 (0.8758, 1.5052) 0.3172	0.3271
Negative	40	22 (55.0)	18 (45.0)	2.9 (0.9, 13.5)	18	7 (38.9)	11 (61.1)	6.0 (1.6, NE)	1.4167 (0.5965, 3.3647) 0.4299	0.4392

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.4060
HER2 IHC 1+	214	121 (56.5)	93 (43.5)	4.2 (2.9, 8.2)	107	47 (43.9)	60 (56.1)	5.8 (3.2, 11.3)	1.0267 (0.7299, 1.4443) 0.8795	0.8861	
HER2 IHC 2+/ISH Negative	159	98 (61.6)	61 (38.4)	4.2 (2.8, 5.7)	77	35 (45.5)	42 (54.5)	5.9 (3.2, NE)	1.2508 (0.8490, 1.8428) 0.2576	0.2634	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.7023
1	221	135 (61.1)	86 (38.9)	3.5 (2.9, 5.7)	100	49 (49.0)	51 (51.0)	4.9 (2.9, 11.2)	1.0548 (0.7589, 1.4662) 0.7507	0.7551
>=2	151	83 (55.0)	68 (45.0)	4.8 (2.8, 10.0)	83	33 (39.8)	50 (60.2)	6.0 (4.4, NE)	1.1919 (0.7928, 1.7920) 0.3988	0.4057

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.3818
Yes	235	139 (59.1)	96 (40.9)	4.3 (2.9, 5.7)	118	50 (42.4)	68 (57.6)	4.9 (3.2, NE)	1.1385 (0.8222, 1.5767) 0.4348	0.4446	
No	98	55 (56.1)	43 (43.9)	5.6 (2.9, 14.5)	48	25 (52.1)	23 (47.9)	6.1 (2.9, 11.2)	0.8751 (0.5422, 1.4124) 0.5850	0.5834	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9926
<65	290	171 (59.0)	119 (41.0)	4.2 (2.9, 5.7)	136	58 (42.6)	78 (57.4)	5.6 (3.2, 11.2)	1.1419 (0.8457, 1.5419) 0.3863	0.4007	
>=65	83	48 (57.8)	35 (42.2)	4.4 (2.9, 8.5)	48	24 (50.0)	24 (50.0)	6.7 (2.8, 11.3)	1.1071 (0.6748, 1.8165) 0.6871	0.6832	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5128
<75	359	211 (58.8)	148 (41.2)	4.2 (2.9, 5.6)	175	77 (44.0)	98 (56.0)	5.8 (3.8, 8.4)	1.0984 (0.8442, 1.4293) 0.4847	0.4942	
>=75	14	8 (57.1)	6 (42.9)	5.8 (1.4, NE)	9	5 (55.6)	4 (44.4)	6.7 (1.5, NE)	2.1215 (0.6315, 7.1268) 0.2238	0.2135	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Race										0.4094
White	176	98 (55.7)	78 (44.3)	4.3 (2.8, 6.2)	91	40 (44.0)	51 (56.0)	4.7 (3.1, 6.7)	1.0089 (0.6958, 1.4629) 0.9626	0.9641
Non-White	197	121 (61.4)	76 (38.6)	4.2 (2.9, 7.1)	92	42 (45.7)	50 (54.3)	7.5 (3.3, 11.3)	1.1921 (0.8365, 1.6988) 0.3309	0.3389

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.1852
Asia	147	94 (63.9)	53 (36.1)	4.2 (2.8, 7.1)	66	30 (45.5)	36 (54.5)	8.3 (3.0, 11.3)	1.2581 (0.8318, 1.9029) 0.2767	0.2810	
North America	60	34 (56.7)	26 (43.3)	3.0 (1.5, 9.7)	33	10 (30.3)	23 (69.7)	NE (1.9, NE)	1.6077 (0.7859, 3.2888) 0.1935	0.1884	
Europe + Israel	166	91 (54.8)	75 (45.2)	4.3 (2.8, 8.5)	85	42 (49.4)	43 (50.6)	4.7 (2.8, 6.7)	0.8922 (0.6164, 1.2912) 0.5452	0.5423	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.7656
0	200	120 (60.0)	80 (40.0)	4.3 (2.9, 7.1)	105	44 (41.9)	61 (58.1)	4.9 (3.2, NE)	1.1001 (0.7765, 1.5584) 0.5915	0.5868	
1	173	99 (57.2)	74 (42.8)	4.2 (2.8, 8.3)	79	38 (48.1)	41 (51.9)	5.9 (3.3, 11.3)	1.1468 (0.7864, 1.6723) 0.4766	0.4931	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.1594
0	60	37 (61.7)	23 (38.3)	1.7 (1.4, 5.6)	34	13 (38.2)	21 (61.8)	6.0 (2.9, NE)	1.6224 (0.8573, 3.0704)	0.1332
1	108	54 (50.0)	54 (50.0)	7.1 (2.9, 11.1)	51	29 (56.9)	22 (43.1)	3.3 (1.4, 6.1)	0.7298 (0.4639, 1.1481)	0.1694
2	115	75 (65.2)	40 (34.8)	4.3 (2.8, 5.7)	54	23 (42.6)	31 (57.4)	6.7 (2.8, NE)	1.1839 (0.7375, 1.9004)	0.4897

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	53 (58.9)	37 (41.1)	4.3 (2.8, 8.5)	45	17 (37.8)	28 (62.2)	8.3 (3.2, NE)	1.3540 (0.7809, 2.3478) 0.2804	0.2831

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.4422
PD	174	94 (54.0)	80 (46.0)	4.3 (2.9, 8.2)	85	32 (37.6)	53 (62.4)	7.5 (3.2, NE)	1.2342 (0.8243, 1.8479) 0.3070	0.3072
PR	48	29 (60.4)	19 (39.6)	8.5 (2.9, 16.7)	22	12 (54.5)	10 (45.5)	4.9 (1.4, 8.4)	0.6590 (0.3293, 1.3188) 0.2388	0.2311
SD	82	52 (63.4)	30 (36.6)	4.2 (2.8, 5.8)	55	27 (49.1)	28 (50.9)	5.9 (3.1, 11.3)	1.2013 (0.7523, 1.9183) 0.4424	0.4523

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.0982
Yes	37	22 (59.5)	15 (40.5)	2.9 (1.5, 12.5)	15	3 (20.0)	12 (80.0)	NE (0.9, NE)	2.7304 (0.8169, 9.1260) 0.1028	0.0884	
No	336	197 (58.6)	139 (41.4)	4.3 (3.0, 5.7)	169	79 (46.7)	90 (53.3)	5.8 (3.3, 8.3)	1.0511 (0.8075, 1.3682) 0.7111	0.7231	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.6756
Yes	24	14 (58.3)	10 (41.7)	4.2 (1.5, 12.5)	8	3 (37.5)	5 (62.5)	5.9 (0.7, NE)	1.3850 (0.3973, 4.8286) 0.6092	0.6122	
No	349	205 (58.7)	144 (41.3)	4.2 (2.9, 5.6)	176	79 (44.9)	97 (55.1)	5.8 (4.4, 8.4)	1.1054 (0.8506, 1.4365) 0.4535	0.4642	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.2622
Normal Function	202	124 (61.4)	78 (38.6)	4.2 (2.9, 5.6)	87	42 (48.3)	45 (51.7)	3.8 (1.9, 11.2)	0.9577 (0.6729, 1.3630) 0.8103	0.7921	
Mild Impairment	123	69 (56.1)	54 (43.9)	3.4 (1.7, 8.6)	69	31 (44.9)	38 (55.1)	5.8 (3.1, 8.3)	1.1129 (0.7251, 1.7082) 0.6246	0.6385	
Moderate Impairment	41	25 (61.0)	16 (39.0)	5.8 (3.0, 15.2)	23	8 (34.8)	15 (65.2)	11.3 (4.5, NE)	1.8244 (0.8174, 4.0717) 0.1422	0.1342	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.7465
Normal Function	170	107 (62.9)	63 (37.1)	4.2 (2.9, 5.8)	98	48 (49.0)	50 (51.0)	5.9 (3.2, 8.3)	1.0646 (0.7544, 1.5024) 0.7217	0.7371	
Mild Impairment	195	111 (56.9)	84 (43.1)	3.5 (2.8, 8.5)	84	34 (40.5)	50 (59.5)	5.6 (2.9, NE)	1.1919 (0.8099, 1.7541) 0.3733	0.3761	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline visceral disease										0.5454
Yes	332	196 (59.0)	136 (41.0)	4.2 (2.9, 5.6)	157	68 (43.3)	89 (56.7)	5.9 (3.3, 11.3)	1.1574 (0.8768, 1.5279) 0.3020	0.3056
No	41	23 (56.1)	18 (43.9)	5.1 (2.8, 16.7)	27	14 (51.9)	13 (48.1)	5.8 (1.6, NE)	0.8167 (0.4087, 1.6323) 0.5666	0.5534

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)									0.5576
Positive	331	195 (58.9)	136 (41.1) (3.0, 5.7)	163	72 (44.2)	91 (55.8) (3.3, 11.2)	1.0889 (0.8293, 1.4298) 0.5398	0.5469	
Negative	42	24 (57.1)	18 (42.9) (1.4, 16.7)	21	10 (47.6)	11 (52.4) (1.5, NE)	1.3654 (0.6451, 2.8902) 0.4156	0.4248	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.1283
Positive	333	193 (58.0)	140 (42.0)	4.4 (3.1, 6.2)	166	75 (45.2)	91 (54.8)	5.8 (3.3, 8.4)	1.0420 (0.7962, 1.3636) 0.7644	0.7716	
Negative	40	26 (65.0)	14 (35.0)	1.5 (1.4, 2.9)	18	7 (38.9)	11 (61.1)	5.9 (1.5, NE)	2.0723 (0.8937, 4.8052) 0.0895	0.0841	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.5072
HER2 IHC 1+	214	97 (45.3)	117 (54.7)	9.8 (7.1, 20.9)	107	33 (30.8)	74 (69.2)	11.4 (9.0, NE)	1.1913 (0.7999, 1.7742) 0.3891	0.3919	
HER2 IHC 2+/ISH Negative	159	76 (47.8)	83 (52.2)	9.0 (4.4, NE)	77	23 (29.9)	54 (70.1)	13.3 (8.6, NE)	1.5203 (0.9523, 2.4271) 0.0792	0.0782	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.9367
1	221	107 (48.4)	114 (51.6)	9.0 (5.6, 20.9)	100	32 (32.0)	68 (68.0)	13.3 (9.0, NE)	1.3388 (0.9009, 1.9896) 0.1489	0.1469
>=2	151	66 (43.7)	85 (56.3)	12.5 (5.6, NE)	83	24 (28.9)	59 (71.1)	14.4 (8.6, NE)	1.3154 (0.8214, 2.1063) 0.2539	0.2607

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.0388
Yes	235	119 (50.6)	116 (49.4)	7.6 (4.4, 10.3)	118	32 (27.1)	86 (72.9)	13.3 (9.0, NE)	1.6253 (1.0983, 2.4053) 0.0152	0.0143	
No	98	35 (35.7)	63 (64.3)	NE (16.1, NE)	48	17 (35.4)	31 (64.6)	14.4 (3.0, NE)	0.8210 (0.4579, 1.4720) 0.5079	0.5025	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2880
<65	290	140 (48.3)	150 (51.7)	9.2 (5.8, 16.1)	136	39 (28.7)	97 (71.3)	13.3 (9.0, NE)	1.4364 (1.0055, 2.0520) 0.0466	0.0466	
>=65	83	33 (39.8)	50 (60.2)	14.1 (5.6, NE)	48	17 (35.4)	31 (64.6)	14.4 (4.2, NE)	1.0108 (0.5607, 1.8223) 0.9715	0.9686	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5768
<75	359	166 (46.2)	193 (53.8)	9.6 (7.0, 20.9)	175	53 (30.3)	122 (69.7)	13.3 (9.0, NE)	1.2972 (0.9505, 1.7705) 0.1011	0.1022	
>=75	14	7 (50.0)	7 (50.0)	14.1 (0.9, NE)	9	3 (33.3)	6 (66.7)	14.4 (0.8, NE)	1.6313 (0.4174, 6.3746) 0.4816	0.4773	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.2714
White	176	88 (50.0)	88 (50.0)	7.0 (3.0, 12.5)	91	26 (28.6)	65 (71.4)	13.3 (9.0, NE)	1.5688 (1.0098, 2.4373) 0.0451	0.0435	
Non-White	197	85 (43.1)	112 (56.9)	15.3 (8.3, NE)	92	30 (32.6)	62 (67.4)	14.4 (9.0, NE)	1.1221 (0.7386, 1.7048) 0.5892	0.5964	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.4261
Asia	147	63 (42.9)	84 (57.1)	NE (7.6, NE)	66	23 (34.8)	43 (65.2)	14.4 (8.6, NE)	1.0510 (0.6509, 1.6972) 0.8387	0.8493	
North America	60	27 (45.0)	33 (55.0)	5.6 (3.0, 9.8)	33	8 (24.2)	25 (75.8)	13.3 (NE, NE)	1.4872 (0.6707, 3.2978) 0.3287	0.3255	
Europe + Israel	166	83 (50.0)	83 (50.0)	8.3 (3.1, 15.3)	85	25 (29.4)	60 (70.6)	11.4 (9.0, NE)	1.5670 (0.9982, 2.4601) 0.0509	0.0499	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.3595
0	200	93 (46.5)	107 (53.5)	9.8 (7.0, NE)	105	33 (31.4)	72 (68.6)	11.4 (9.0, NE)	1.1775 (0.7902, 1.7546) 0.4220	0.4227	
1	173	80 (46.2)	93 (53.8)	9.2 (5.6, 15.3)	79	23 (29.1)	56 (70.9)	13.3 (8.6, NE)	1.5198 (0.9524, 2.4253) 0.0792	0.0790	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.2774
0	60	25 (41.7)	35 (58.3)	12.5 (5.4, NE)	34	10 (29.4)	24 (70.6)	NE (5.3, NE)	1.1898 (0.5693, 2.4869) 0.6440	0.6472	
1	108	49 (45.4)	59 (54.6)	9.6 (3.5, NE)	51	17 (33.3)	34 (66.7)	NE (4.2, NE)	1.2390 (0.7111, 2.1588) 0.4493	0.4468	
2	115	58 (50.4)	57 (49.6)	8.3 (4.4, 15.3)	54	11 (20.4)	43 (79.6)	NE (NE, NE)	2.1585 (1.1273, 4.1330) 0.0203	0.0172	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	41 (45.6)	49 (54.4)	11.3 (4.9, NE)	45	18 (40.0)	27 (60.0)	9.3 (5.1, 14.4)	0.9256 (0.5293, 1.6184) 0.7862	0.7769

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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 [c] Two-sided p-value from unstratified log-rank test.  
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Common Symptoms/Diarrhea

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.1329
PD	174	82 (47.1)	92 (52.9)	7.6 (4.6, 14.1)	85	21 (24.7)	64 (75.3)	11.4 (11.4, NE)	1.7490 (1.0794, 2.8340) 0.0232	0.0221
PR	48	13 (27.1)	35 (72.9)	NE (NE, NE)	22	7 (31.8)	15 (68.2)	9.0 (3.0, NE)	0.6478 (0.2562, 1.6380) 0.3590	0.3469
SD	82	45 (54.9)	37 (45.1)	7.0 (2.8, 10.3)	55	19 (34.5)	36 (65.5)	NE (9.0, NE)	1.4537 (0.8494, 2.4879) 0.1724	0.1680

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Common Symptoms/Diarrhea

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.2413
Yes	37	18 (48.6)	19 (51.4)	9.4 (3.0, NE)	15	2 (13.3)	13 (86.7)	NE (1.5, NE)	2.7282 (0.6272, 11.8676)	0.1619
No	336	155 (46.1)	181 (53.9)	9.6 (7.0, 20.9)	169	54 (32.0)	115 (68.0)	13.3 (9.0, NE)	1.2749 (0.9338, 1.7406)	0.1281

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Baseline CNS metastases											0.0185
Yes	24	12 (50.0)	12 (50.0)	9.6 (1.6, NE)	8	0	8 (100)	NE (NE, NE)	NE (NE, NE) 0.9931	0.0441	
No	349	161 (46.1)	188 (53.9)	9.7 (7.0, 20.9)	176	56 (31.8)	120 (68.2)	13.3 (9.0, NE)	1.2546 (0.9240, 1.7034) 0.1461	0.1483	

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Renal function at baseline										0.0148
Normal Function	202	100 (49.5)	102 (50.5)	8.3 (5.6, 16.1)	87	17 (19.5)	70 (80.5)	NE (13.3, NE)	2.2863 (1.3653, 3.8285) 0.0017	0.0013
Mild Impairment	123	56 (45.5)	67 (54.5)	11.3 (5.4, NE)	69	26 (37.7)	43 (62.3)	9.0 (2.9, NE)	0.9149 (0.5690, 1.4709) 0.7135	0.7118
Moderate Impairment	41	16 (39.0)	25 (61.0)	NE (3.0, NE)	23	11 (47.8)	12 (52.2)	11.4 (1.5, NE)	0.8667 (0.4020, 1.8690) 0.7153	0.7181

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.6547
Normal Function	170	85 (50.0)	85 (50.0)	9.0 (5.1, NE)	98	30 (30.6)	68 (69.4)	14.4 (9.0, NE)	1.4338 (0.9439, 2.1779) 0.0912	0.0900	
Mild Impairment	195	87 (44.6)	108 (55.4)	11.1 (5.6, 21.7)	84	25 (29.8)	59 (70.2)	13.3 (5.3, NE)	1.2146 (0.7754, 1.9026) 0.3959	0.3967	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline visceral disease										0.1225
Yes	332	154 (46.4)	178 (53.6)	9.6 (7.1, 16.1)	157	43 (27.4)	114 (72.6)	14.4 (11.4, NE)	1.4802 (1.0539, 2.0790) 0.0236	0.0228
No	41	19 (46.3)	22 (53.7)	7.0 (3.0, NE)	27	13 (48.1)	14 (51.9)	5.9 (1.5, NE)	0.8328 (0.4096, 1.6932) 0.6133	0.6052

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.5058
Positive	331	155 (46.8)	176 (53.2)	9.6 (7.0, 20.9)	163	47 (28.8)	116 (71.2)	14.4 (9.3, NE)	1.3861 (0.9985, 1.9240) 0.0510	0.0503	
Negative	42	18 (42.9)	24 (57.1)	8.9 (2.8, NE)	21	9 (42.9)	12 (57.1)	5.9 (3.0, NE)	1.0105 (0.4494, 2.2721) 0.9798	0.9983	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.8827
Positive	333	154 (46.2)	179 (53.8)	9.7 (7.0, 20.9)	166	49 (29.5)	117 (70.5)	14.4 (9.3, NE)	1.3419 (0.9714, 1.8537) 0.0744	0.0740	
Negative	40	19 (47.5)	21 (52.5)	7.6 (2.8, NE)	18	7 (38.9)	11 (61.1)	9.0 (3.2, NE)	1.2141 (0.5055, 2.9159) 0.6643	0.6766	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.6670
HER2 IHC 1+	214	63 (29.4)	151 (70.6)	NE (16.4, NE)	107	27 (25.2)	80 (74.8)	18.5 (11.3, NE)	0.7854 (0.4950, 1.2463) 0.3052	0.3032
HER2 IHC 2+/ISH Negative	159	43 (27.0)	116 (73.0)	NE (16.5, NE)	77	21 (27.3)	56 (72.7)	NE (6.1, NE)	0.7523 (0.4433, 1.2769) 0.2917	0.2869

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.7850
1	221	60 (27.1)	161 (72.9)	NE (NE, NE)	100	26 (26.0)	74 (74.0)	NE (11.3, NE)	0.8257 (0.5184, 1.3152) 0.4201	0.4196
>=2	151	45 (29.8)	106 (70.2)	NE (13.6, NE)	83	22 (26.5)	61 (73.5)	18.5 (6.1, NE)	0.6825 (0.4034, 1.1548) 0.1546	0.1509

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6									0.5651
Yes	235	61 (26.0)	174 (74.0) (16.5, NE)	118	29 (24.6)	89 (75.4) (18.5, NE)	0.7626 (0.4865, 1.1953) 0.2372	0.2357	
No	98	35 (35.7)	63 (64.3) (12.0, NE)	48	13 (27.1)	35 (72.9) (9.3, NE)	0.9665 (0.5054, 1.8484) 0.9180	0.9105	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Age										0.4081
<65	290	85 (29.3)	205 (70.7)	NE (16.5, NE)	136	38 (27.9)	98 (72.1)	NE (6.9, NE)	0.7276 (0.4930, 1.0737) 0.1092	0.1063
>=65	83	21 (25.3)	62 (74.7)	NE (11.7, NE)	48	10 (20.8)	38 (79.2)	18.5 (11.3, NE)	0.8749 (0.4040, 1.8946) 0.7345	0.7365

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Age											
<75	359	101 (28.1)	258 (71.9)	NE (NE, NE)	175	45 (25.7)	130 (74.3)	18.5 (18.5, NE)	0.7596 (0.5309, 1.0870)	0.1305	0.5801
>=75	14	5 (35.7)	9 (64.3)	NE (1.6, NE)	9	3 (33.3)	6 (66.7)	11.3 (1.4, NE)	1.1756 (0.2798, 4.9388)	0.8250	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.8717
White	176	48 (27.3)	128 (72.7)	NE (NE, NE)	91	23 (25.3)	68 (74.7)	18.5 (6.0, NE)	0.7936 (0.4778, 1.3181) 0.3718	0.3698	
Non-White	197	58 (29.4)	139 (70.6)	NE (16.5, NE)	92	25 (27.2)	67 (72.8)	NE (9.3, NE)	0.7531 (0.4670, 1.2142) 0.2445	0.2431	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.7647
Asia	147	49 (33.3)	98 (66.7)	NE (14.3, NE)	66	20 (30.3)	46 (69.7)	NE (9.3, NE)	0.7521 (0.4431, 1.2768) 0.2915	0.2915	
North America	60	11 (18.3)	49 (81.7)	NE (NE, NE)	33	7 (21.2)	26 (78.8)	NE (2.7, NE)	0.6969 (0.2677, 1.8143) 0.4595	0.4555	
Europe + Israel	166	46 (27.7)	120 (72.3)	NE (NE, NE)	85	21 (24.7)	64 (75.3)	18.5 (NE, NE)	0.8451 (0.4986, 1.4322) 0.5317	0.5277	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	200	57 (28.5)	143 (71.5)	NE (16.5, NE)	105	25 (23.8)	80 (76.2)	18.5 (18.5, NE)	0.8202 (0.5089, 1.3218) 0.4156	0.4157	0.7928
1	173	49 (28.3)	124 (71.7)	NE (13.6, NE)	79	23 (29.1)	56 (70.9)	11.3 (6.9, NE)	0.7038 (0.4229, 1.1715) 0.1767	0.1731	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.0673
0	60	15 (25.0)	45 (75.0)	NE (10.4, NE)	34	9 (26.5)	25 (73.5)	9.3 (5.9, NE)	0.4971 (0.2088, 1.1837) 0.1144	0.1077
1	108	30 (27.8)	78 (72.2)	NE (12.0, NE)	51	15 (29.4)	36 (70.6)	18.5 (6.1, NE)	0.7707 (0.4122, 1.4410) 0.4146	0.4116
2	115	29 (25.2)	86 (74.8)	NE (NE, NE)	54	17 (31.5)	37 (68.5)	NE (5.1, NE)	0.5641 (0.3057, 1.0410) 0.0671	0.0633

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	32 (35.6)	58 (64.4)	NE (11.3, NE)	45	7 (15.6)	38 (84.4)	NE (NE, NE)	1.7357 (0.7590, 3.9694) 0.1914	0.1865

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.8535
PD	174	44 (25.3)	130 (74.7)	NE (16.5, NE)	85	22 (25.9)	63 (74.1)	18.5 (6.9, NE)	0.7307 (0.4334, 1.2319) 0.2391	0.2341
PR	48	17 (35.4)	31 (64.6)	NE (10.4, NE)	22	5 (22.7)	17 (77.3)	NE (1.7, NE)	0.8808 (0.3201, 2.4232) 0.8058	0.8123
SD	82	24 (29.3)	58 (70.7)	NE (13.1, NE)	55	17 (30.9)	38 (69.1)	11.3 (6.1, NE)	0.6482 (0.3438, 1.2220) 0.1801	0.1778

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.1474
Yes	37	10 (27.0)	27 (73.0)	NE (8.8, NE)	15	1 (6.7)	14 (93.3)	NE (NE, NE)	2.7337 (0.3451, 21.6577) 0.3409	0.3210
No	336	96 (28.6)	240 (71.4)	NE (16.5, NE)	169	47 (27.8)	122 (72.2)	18.5 (11.3, NE)	0.7226 (0.5059, 1.0322) 0.0742	0.0723

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.0540
Yes	24	6 (25.0)	18 (75.0)	16.5 (7.1, NE)	8	0	8 (100)	NE (NE, NE)	0.9955	0.2048
No	349	100 (28.7)	249 (71.3)	NE (NE, NE)	176	48 (27.3)	128 (72.7)	18.5 (11.3, NE)	0.7456 (0.5248, 1.0593)	0.0994

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.2506
Normal Function	202	64 (31.7)	138 (68.3)	NE (16.5, NE)	87	23 (26.4)	64 (73.6)	NE (9.3, NE)	0.8916 (0.5503, 1.4445) 0.6412	0.6369	
Mild Impairment	123	29 (23.6)	94 (76.4)	NE (14.3, NE)	69	19 (27.5)	50 (72.5)	NE (6.0, NE)	0.4601 (0.2498, 0.8474) 0.0127	0.0112	
Moderate Impairment	41	12 (29.3)	29 (70.7)	NE (11.2, NE)	23	6 (26.1)	17 (73.9)	18.5 (7.0, NE)	1.0841 (0.4036, 2.9123) 0.8727	0.8741	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.4083
Normal Function	170	52 (30.6)	118 (69.4)	NE (16.5, NE)	98	30 (30.6)	68 (69.4)	NE (6.9, NE)	0.6850 (0.4333, 1.0831) 0.1055	0.1033	
Mild Impairment	195	54 (27.7)	141 (72.3)	NE (16.4, NE)	84	18 (21.4)	66 (78.6)	18.5 (11.3, NE)	0.9174 (0.5327, 1.5797) 0.7558	0.7507	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline visceral disease										0.0686
Yes	332	94 (28.3)	238 (71.7)	NE (NE, NE)	157	37 (23.6)	120 (76.4)	18.5 (11.3, NE)	0.8930 (0.6072, 1.3133)	0.5623
No	41	12 (29.3)	29 (70.7)	NE (13.1, NE)	27	11 (40.7)	16 (59.3)	5.9 (1.7, NE)	0.3395 (0.1394, 0.8268)	0.0130

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (IXRS)										0.4571
Positive	331	95 (28.7)	236 (71.3)	NE (NE, NE)	163	41 (25.2)	122 (74.8)	18.5 (11.3, NE)	0.8198 (0.5648, 1.1898)	0.2930 0.2958
Negative	42	11 (26.2)	31 (73.8)	NE (8.3, NE)	21	7 (33.3)	14 (66.7)	7.0 (4.4, NE)	0.4678 (0.1725, 1.2684)	0.1253 0.1355

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (derived)										0.5019
Positive	333	95 (28.5)	238 (71.5)	NE (NE, NE)	166	42 (25.3)	124 (74.7)	18.5 (11.3, NE)	0.8129 (0.5617, 1.1766)	0.2695
Negative	40	11 (27.5)	29 (72.5)	NE (8.3, NE)	18	6 (33.3)	12 (66.7)	7.0 (1.7, NE)	0.4656 (0.1652, 1.3122)	0.1375

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

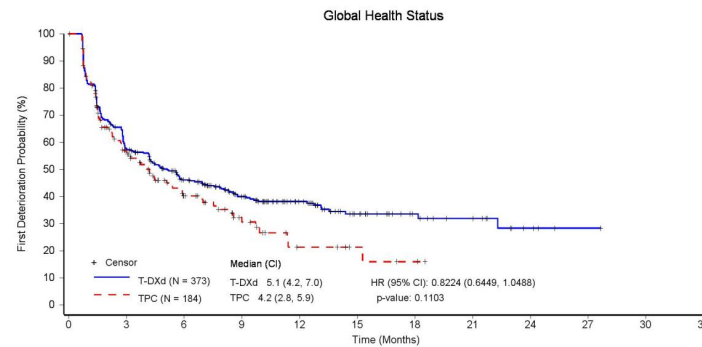
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 10JAN2023 – 19:25; Program name: T3\_EQ5D\_FD\_2\_FAS.sas; Output name: T21C30.rtf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.7.1.3 - EORTC QLQ-C30 - First deterioration 10 points - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - Full Analysis Set

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Patients still at risk:

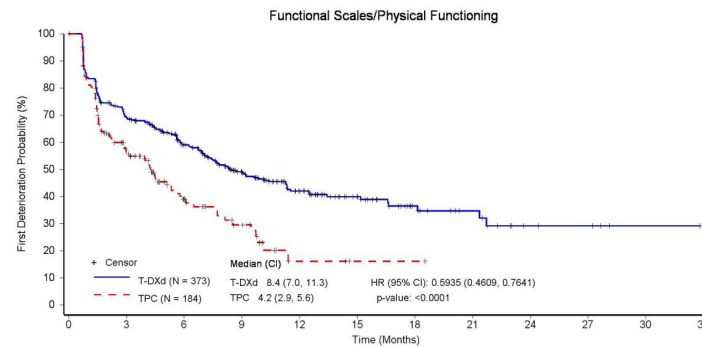
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	193	135	93	60	34	20	13	4	1	0	0
TPC (N = 184)	184	77	38	19	7	4	2	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:26; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F22C30.rtf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.7.1.3 - EORTC QLQ-C30 - First deterioration 10 points - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - Full Analysis Set

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Patients still at risk:

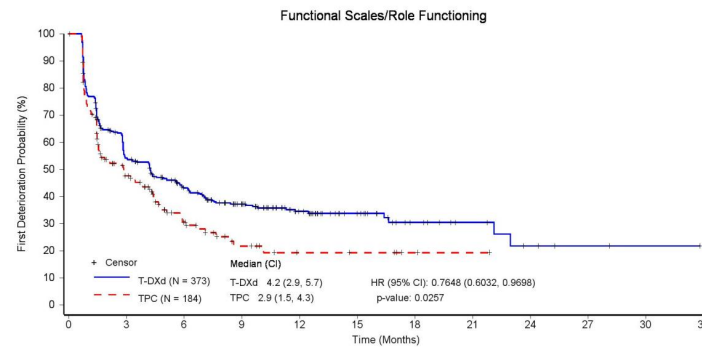
T-DXd (N = 373)	373	232	166	113	68	41	21	13	5	4	1	0
TPC (N = 184)	184	77	33	16	3	1	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:26; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F22C30.rtf

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Patients still at risk:

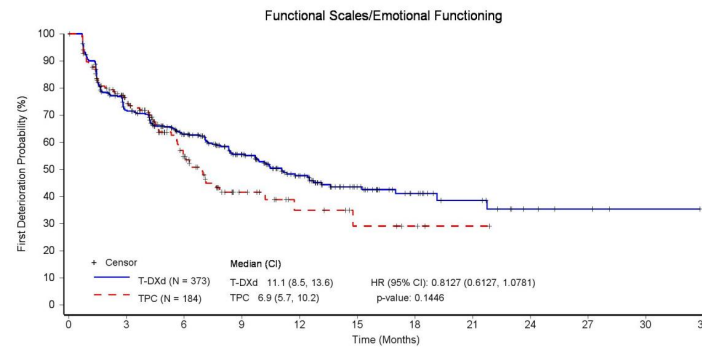
T-DXd (N = 373)	373	178	120	84	48	27	14	8	4	2	1	0
TPC (N = 184)	184	61	26	12	6	5	2	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:26; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F22C30.rtf

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Patients still at risk:

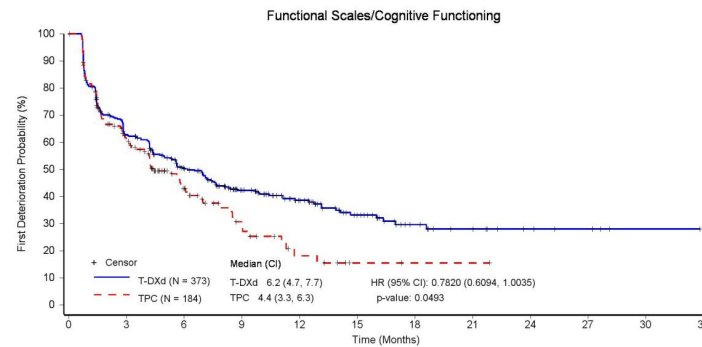
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	239	182	128	79	44	26	14	5	3	1	0
TPC (N = 184)	184	99	46	18	9	5	3	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:26; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F22C30.rtf

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Patients still at risk:

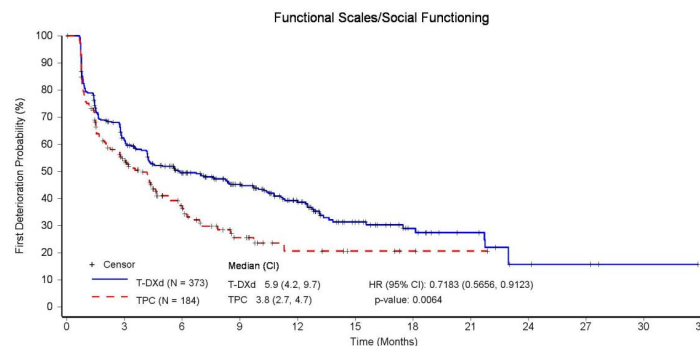
T-DXd (N = 373)	373	205	144	95	62	35	19	11	6	4	1	0
TPC (N = 184)	184	85	37	17	7	2	1	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:26; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F22C30.rtf

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 Data Intelligence – Evidence Generation  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	203	143	105	64	33	19	11	4	3	1	0
TPC (N = 184)	184	79	38	16	7	4	2	1	0	0	0	0

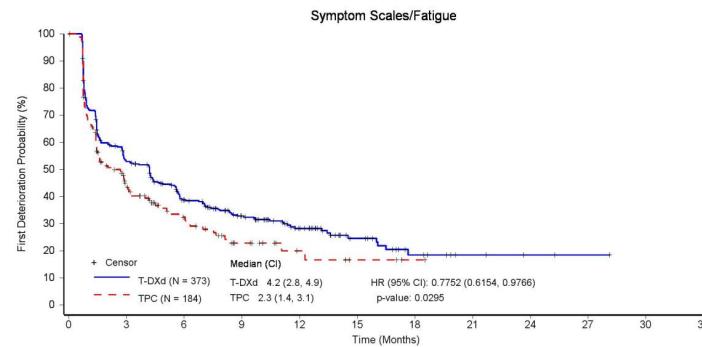
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

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 Run date: 10JAN2023 – 19:26; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F22C30.rtf



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Patients still at risk:

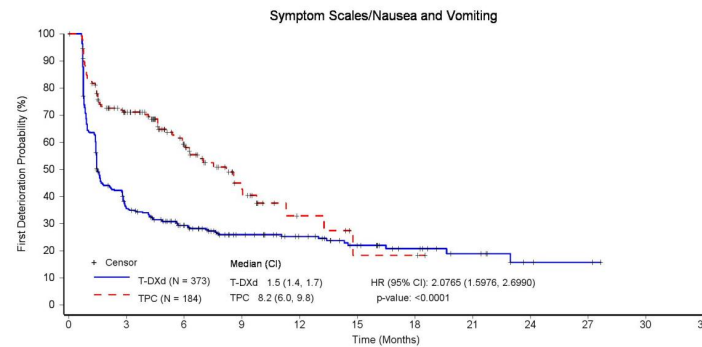
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	176	113	77	45	21	9	4	2	1	0	0
TPC (N = 184)	184	58	29	14	6	3	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 Data Intelligence – Evidence Generation  
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Patients still at risk:

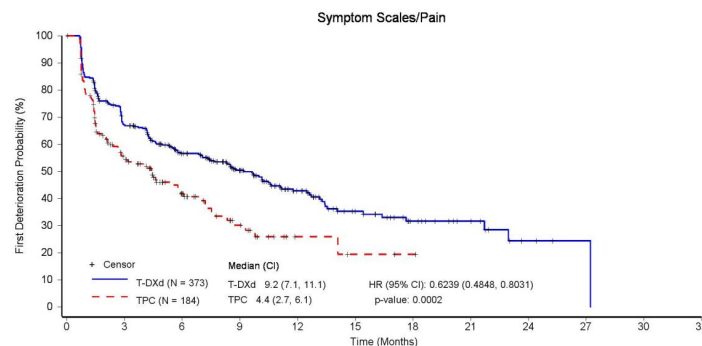
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	116	77	48	36	23	15	9	3	2	0	0
TPC (N = 184)	184	94	50	20	6	2	2	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:26; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F22C30.rtf

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Patients still at risk:

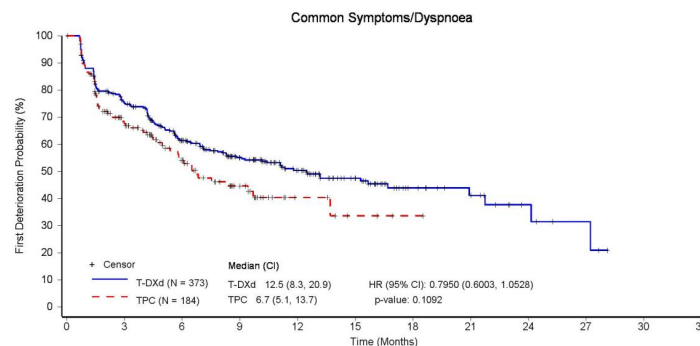
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	220	156	108	62	33	20	12	3	1	0	0
TPC (N = 184)	184	78	38	17	4	2	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 Data Intelligence – Evidence Generation  
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Patients still at risk:

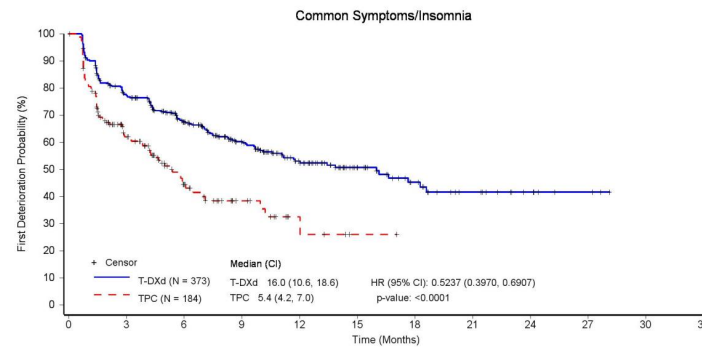
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	248	172	123	81	50	23	15	6	3	0	0
TPC (N = 184)	184	89	47	24	7	3	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:26; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F22C30.rtf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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Patients still at risk:

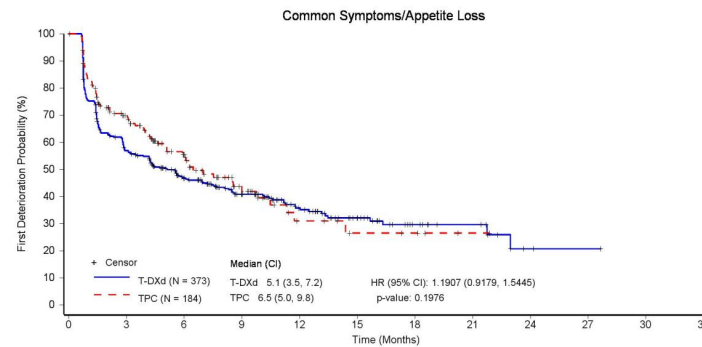
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	256	187	130	82	47	27	14	7	3	0	0
TPC (N = 184)	184	80	35	15	5	1	0	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:26; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F22C30.rtf

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Patients still at risk:

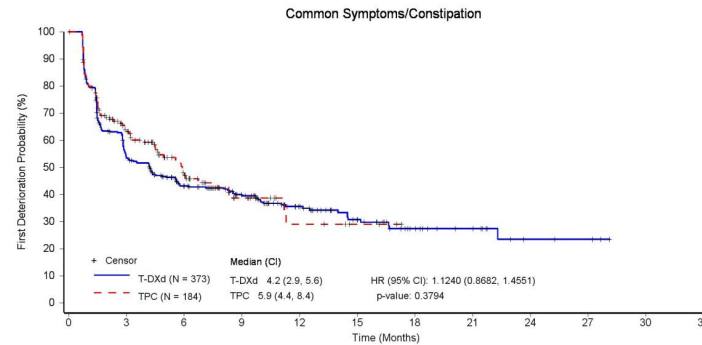
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	192	132	92	55	32	16	10	2	1	0	0
TPC (N = 184)	184	94	50	23	9	5	4	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:26; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F22C30.rtf

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Patients still at risk:

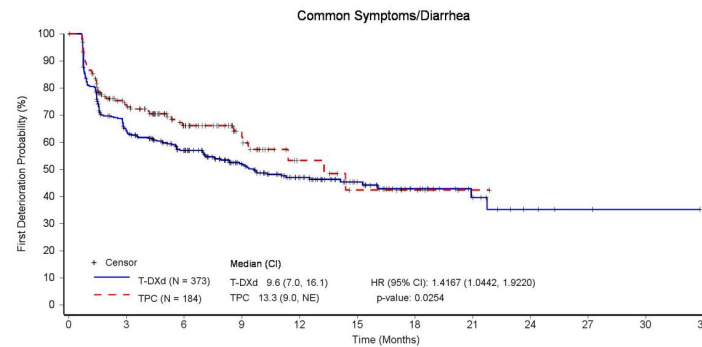
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	177	120	92	56	33	18	12	4	3	0	0
TPC (N = 184)	184	83	42	16	6	3	0	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:26; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F22C30.rtf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	209	159	110	71	40	22	12	4	2	1	0
TPC (N = 184)	184	95	53	29	11	6	4	1	0	0	0	0

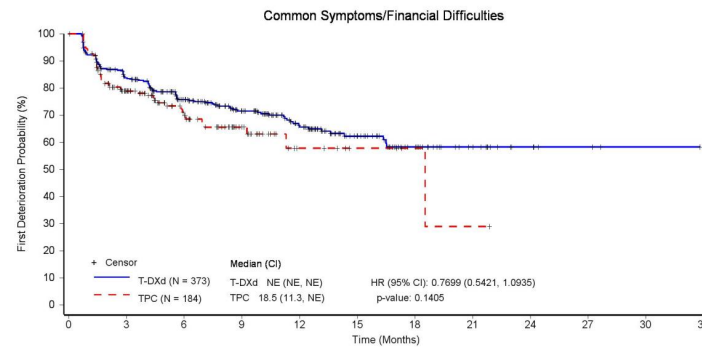
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.7.1.3 - EORTC QLQ-C30 - First deterioration 10 points - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - Full Analysis Set

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Patients still at risk:

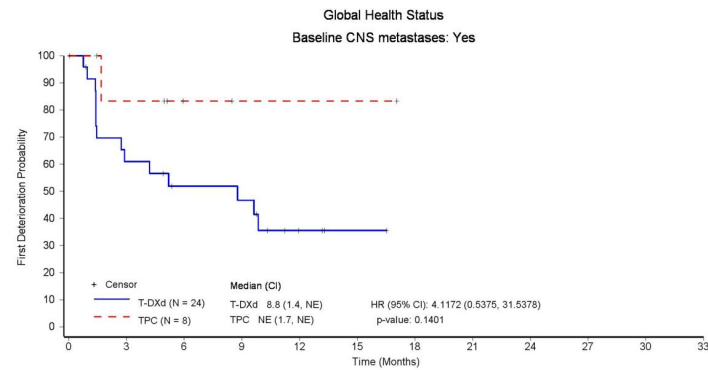
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	269	204	152	99	58	33	15	6	3	1	0
TPC (N = 184)	184	104	57	28	8	4	2	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:26; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F22C30.rtf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.7.1.4 - EORTC QLQ-C30 - First deterioration 10 points - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - Full Analysis Set

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Patients still at risk:

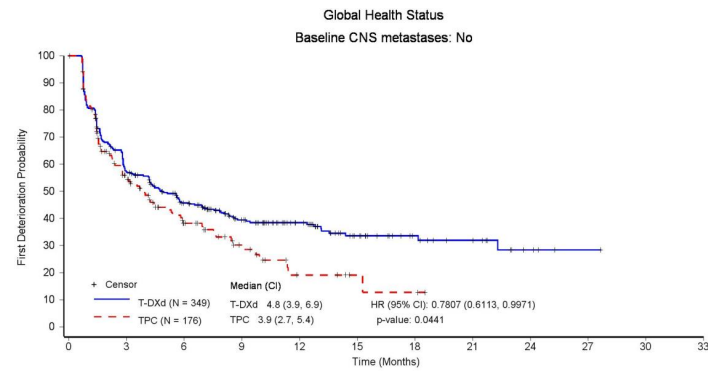
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 24)	24	14	10	9	3	1	0	0	0	0	0	0
TPC (N = 8)	8	5	2	1	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:27; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F23C30.rtf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.7.1.4 - EORTC QLQ-C30 - First deterioration 10 points - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - Full Analysis Set

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Patients still at risk:

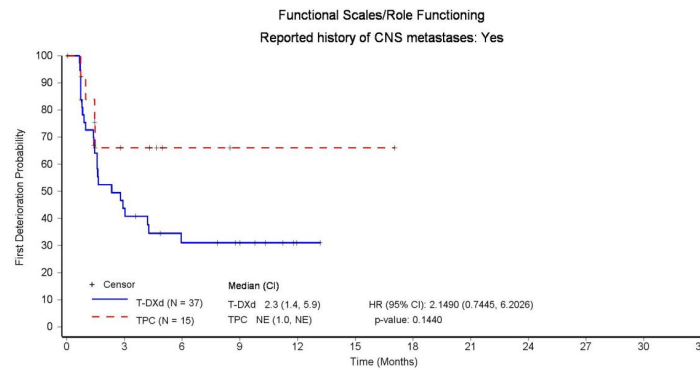
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 349)	349	179	125	84	57	33	20	13	4	1	0	0
TPC (N = 176)	176	72	36	18	6	3	2	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:27; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F23C30.rtf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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 Final



Patients still at risk:

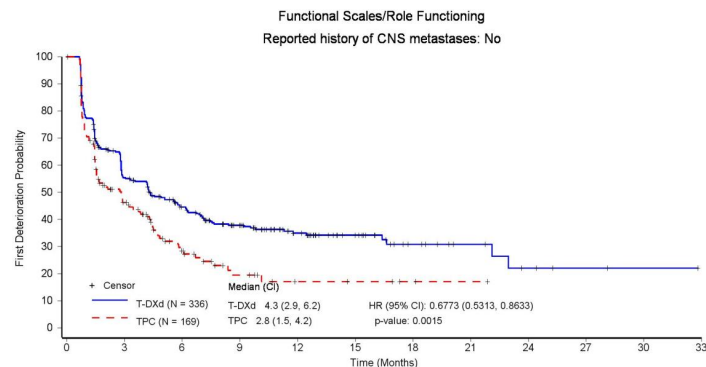
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 37)	37	15	9	7	1	0	0	0	0	0	0	0
TPC (N = 15)	15	5	2	1	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:27; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F23C30.rtf

Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.7.1.4 - EORTC QLQ-C30 - First deterioration 10 points - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - Full Analysis Set

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Patients still at risk:

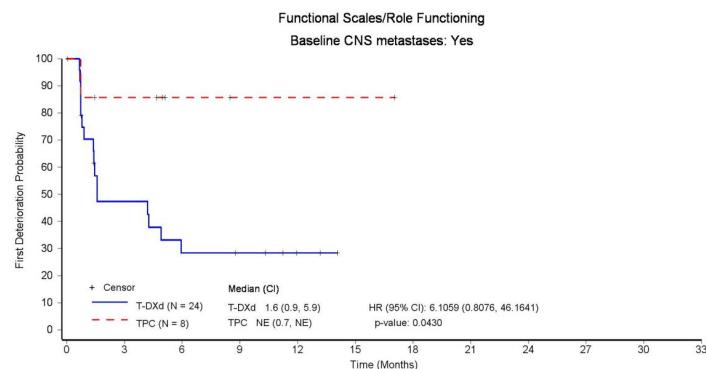
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 336)	336	163	111	77	47	27	14	8	4	2	1	0
TPC (N = 169)	169	56	24	11	5	4	2	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:27; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F23C30.rtf

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Patients still at risk:

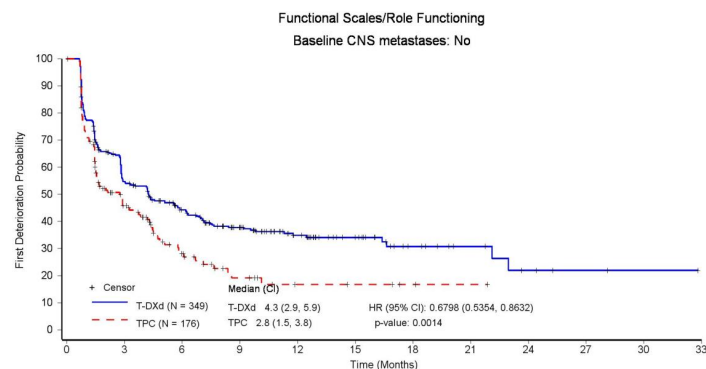
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 24)	24	10	6	5	2	0	0	0	0	0	0	0
TPC (N = 8)	8	5	2	1	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:27; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F23C30.rtf

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Patients still at risk:

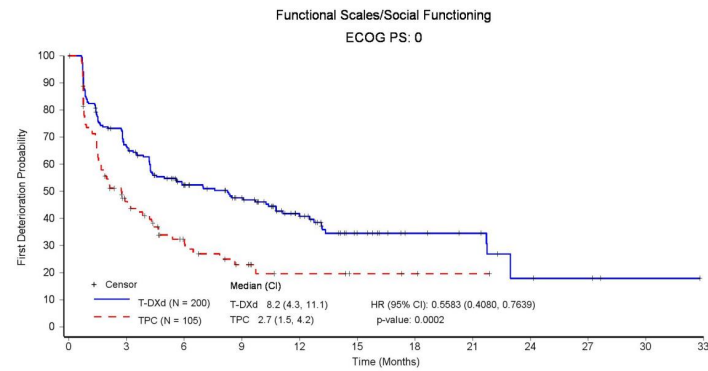
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 349)	349	168	114	79	46	27	14	8	4	2	1	0
TPC (N = 176)	176	56	24	11	5	4	2	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 200)	200	121	84	66	40	20	13	10	4	3	1	0
TPC (N = 105)	105	36	18	10	5	3	2	1	0	0	0	0

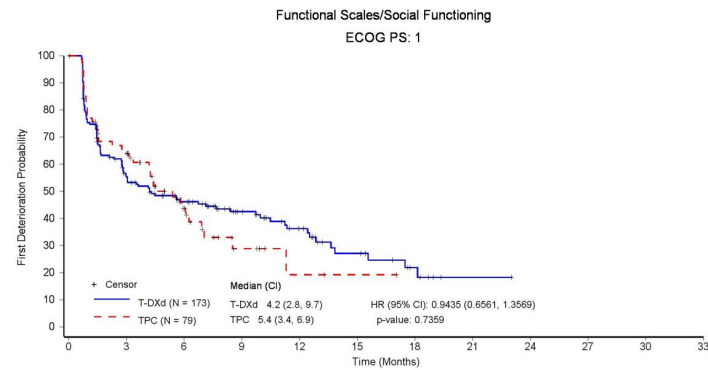
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:27; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F23C30.rtf



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Patients still at risk:

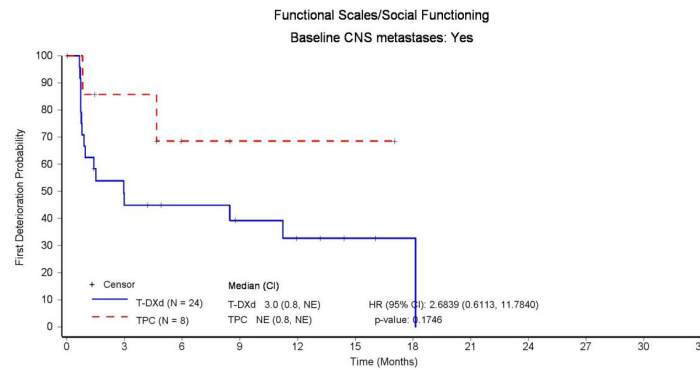
T-DXd (N = 173)	173	82	59	39	24	13	6	1	0	0	0	0
TPC (N = 79)	79	43	20	6	2	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

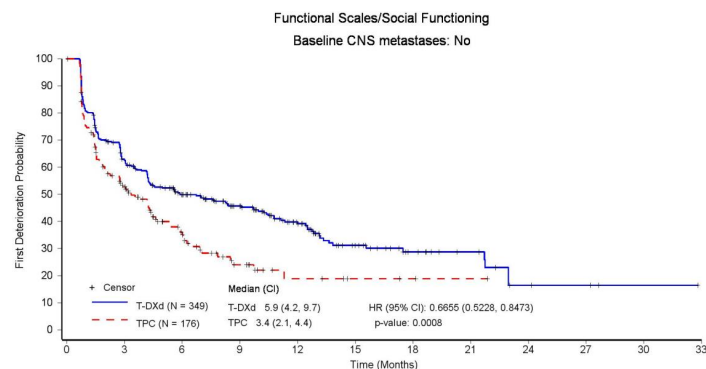
T-DXd (N = 24)	24	10	8	6	4	2	1	0	0	0	0	0
TPC (N = 8)	8	5	2	1	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

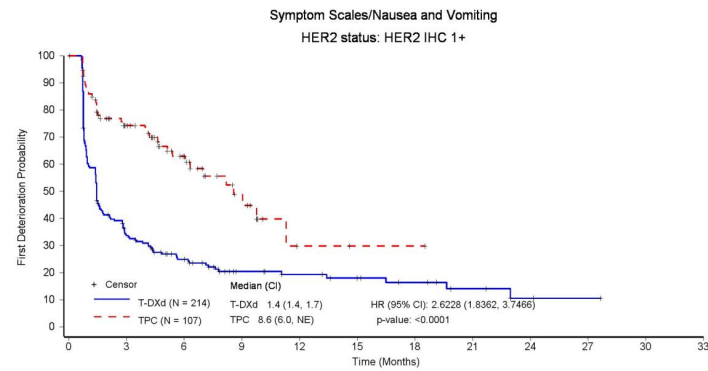
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 349)	349	193	135	99	60	31	18	11	4	3	1	0
TPC (N = 176)	176	74	36	15	6	3	2	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:27; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F23C30.rtf

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Patients still at risk:

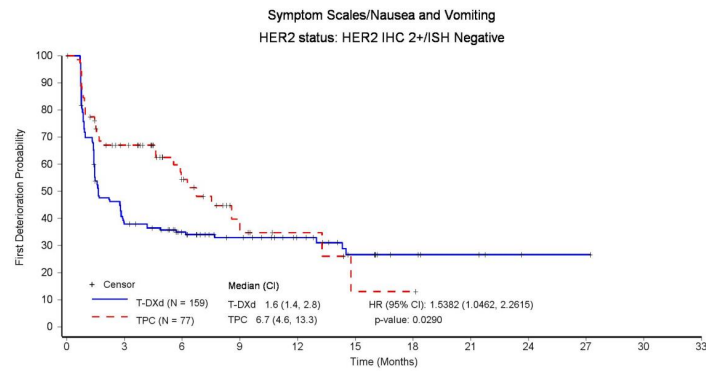
T-DXd (N = 214)	214	61	38	20	16	12	9	5	2	1	0	0
TPC (N = 107)	107	54	31	12	2	1	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:27; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F23C30.rtf

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Patients still at risk:

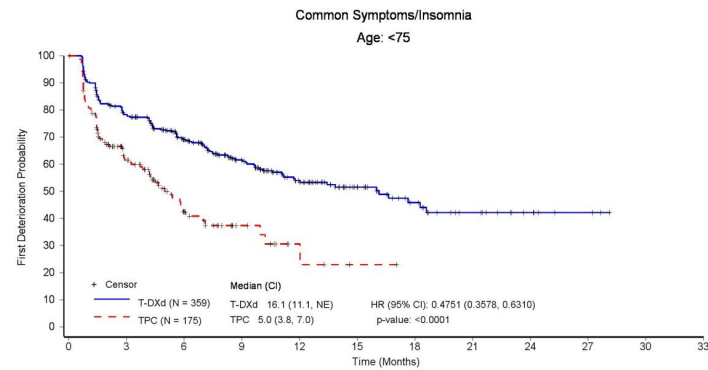
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 159)	159	55	39	28	20	11	6	4	1	1	0	0
TPC (N = 77)	77	40	19	8	4	1	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

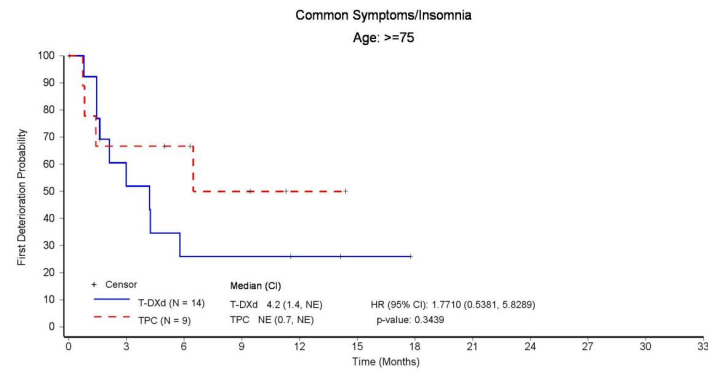
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 359)	359	249	184	127	80	46	27	14	7	3	0	0
TPC (N = 175)	175	74	30	12	4	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 Data Intelligence – Evidence Generation  
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Patients still at risk:

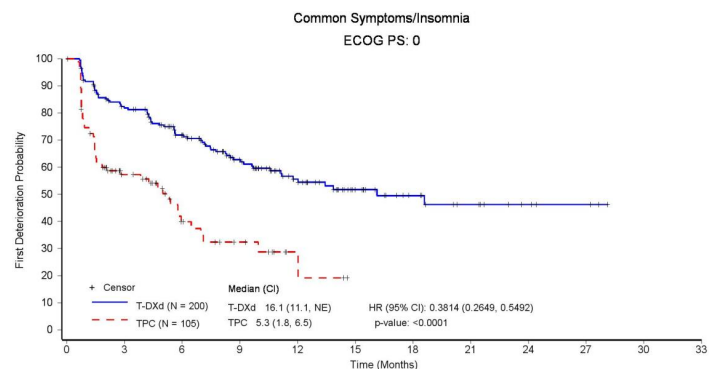
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 14)	14	6	3	3	2	1	0	0	0	0	0	0
TPC (N = 9)	9	6	5	3	1	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 200)	200	148	113	80	49	28	17	10	5	3	0	0
TPC (N = 105)	105	38	17	10	3	0	0	0	0	0	0	0

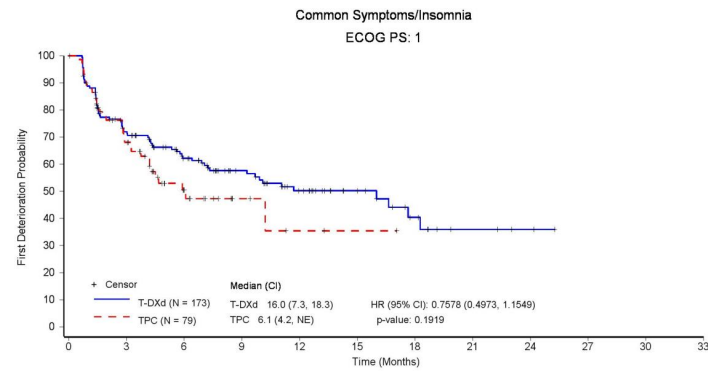
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Patients still at risk:

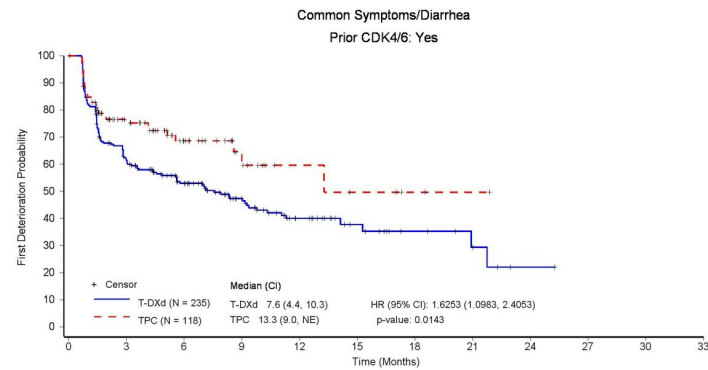
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 173)	173	107	74	50	33	19	10	4	2	0	0	0
TPC (N = 79)	79	42	18	5	2	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

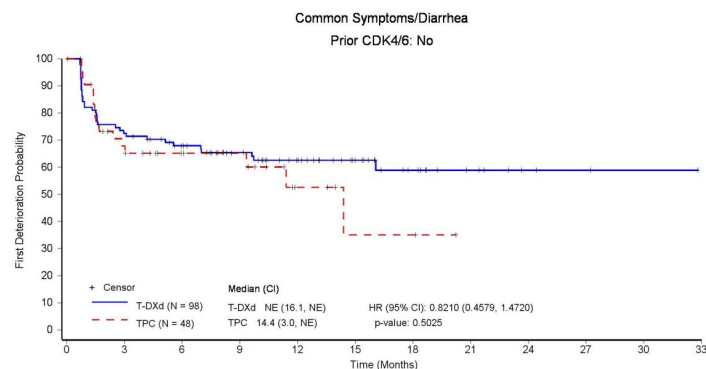
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 235)	235	126	90	56	30	15	8	5	1	0	0	0
TPC (N = 118)	118	59	30	13	6	4	2	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

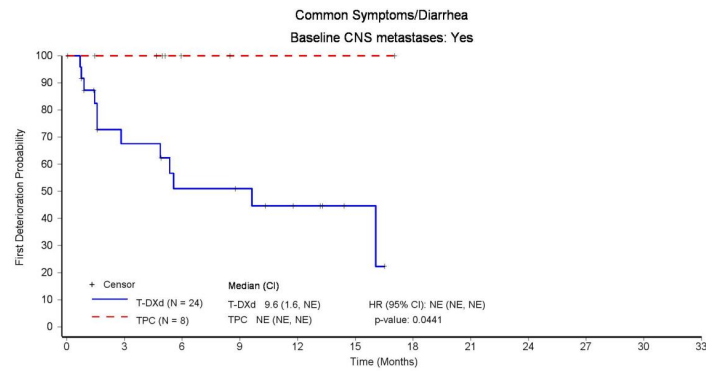
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 98)	98	67	56	47	35	22	13	7	3	2	1	0
TPC (N = 48)	48	25	18	13	5	2	2	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

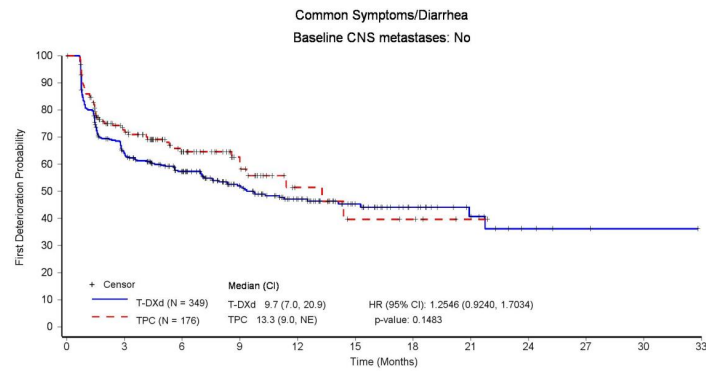
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 24)	24	13	9	8	5	2	0	0	0	0	0	0
TPC (N = 8)	8	6	2	1	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:27; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F23C30.rtf

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Patients still at risk:

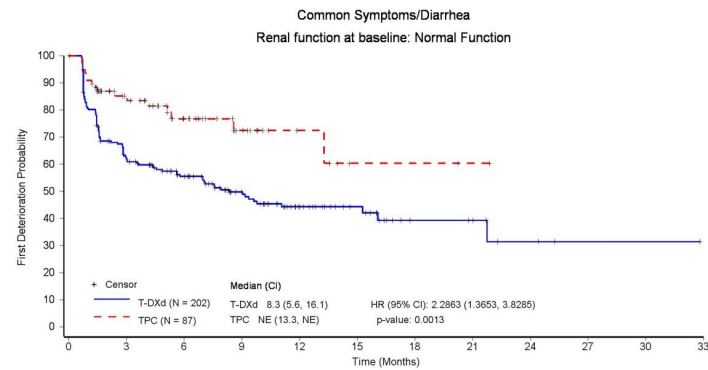
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 349)	349	196	150	102	66	38	22	12	4	2	1	0
TPC (N = 176)	176	89	51	28	10	5	4	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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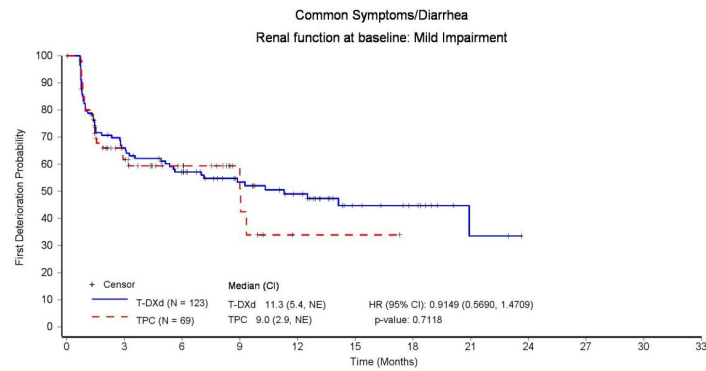
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 202)	202	113	86	57	32	20	8	7	3	1	1	0
TPC (N = 87)	87	48	26	14	6	2	2	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

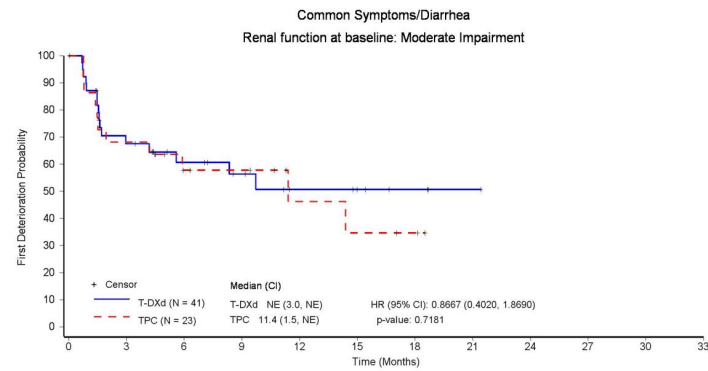
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 123)	123	69	55	39	30	14	10	3	0	0	0	0
TPC (N = 69)	69	29	17	7	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

T-DXd (N = 41)	41	23	16	12	7	5	3	1	0	0	0	0
TPC (N = 23)	23	15	9	8	4	3	2	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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#### Global Health Status

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	160 (42.9)	77 (41.8)	
Number of subjects censored, n (%)	213 (57.1)	107 (58.2)	
Median time to first event (months) [a]	14.4	8.4	
95% Confidence Interval	[9.8, 18.4]	[5.9, 10.8]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.6851
95% Confidence Interval			[0.5174, 0.9073]
p-value			0.0083
Stratified log-rank p-value [c]			0.0078

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Functional Scales/Physical Functioning

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	140 (37.5)	80 (43.5)	
Number of subjects censored, n (%)	233 (62.5)	104 (56.5)	
Median time to first event (months) [a]	16.9	7.5	
95% Confidence Interval	[12.5, NE]	[5.3, 9.8]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.5234
95% Confidence Interval			[0.3935, 0.6962]
p-value			<0.0001
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Functional Scales/Role Functioning

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	159 (42.6)	86 (46.7)	
Number of subjects censored, n (%)	214 (57.4)	98 (53.3)	
Median time to first event (months) [a]	16.0	5.8	
95% Confidence Interval	[9.8, 21.5]	[4.3, 7.7]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.5733
95% Confidence Interval			[0.4367, 0.7527]
p-value			0.0001
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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#### Functional Scales/Emotional Functioning

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	120 (32.2)	49 (26.6)	
Number of subjects censored, n (%)	253 (67.8)	135 (73.4)	
Median time to first event (months) [a]	21.7	11.7	
95% Confidence Interval	[16.7, NE]	[8.4, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.7515
95% Confidence Interval			[0.5320, 1.0617]
p-value			0.1051
Stratified log-rank p-value [c]			0.1047

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Functional Scales/Cognitive Functioning

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	157 (42.1)	82 (44.6)	
Number of subjects censored, n (%)	216 (57.9)	102 (55.4)	
Median time to first event (months) [a]	13.6	6.9	
95% Confidence Interval	[10.8, 17.5]	[5.4, 9.0]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.6015
95% Confidence Interval			[0.4557, 0.7940]
p-value			0.0003
Stratified log-rank p-value [c]			0.0003

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Functional Scales/Social Functioning

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	156 (41.8)	88 (47.8)	
Number of subjects censored, n (%)	217 (58.2)	96 (52.2)	
Median time to first event (months) [a]	13.6	6.0	
95% Confidence Interval	[11.3, 18.2]	[4.6, 7.9]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.5917
95% Confidence Interval			[0.4509, 0.7765]
p-value			0.0002
Stratified log-rank p-value [c]			0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Symptom Scales/Fatigue

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	178 (47.7)	92 (50.0)	
Number of subjects censored, n (%)	195 (52.3)	92 (50.0)	
Median time to first event (months) [a]	11.2	4.9	
95% Confidence Interval	[8.1, 13.3]	[3.2, 7.0]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.6392
95% Confidence Interval			[0.4932, 0.8284]
p-value			0.0007
Stratified log-rank p-value [c]			0.0007

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Symptom Scales/Nausea and Vomiting

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	187 (50.1)	58 (31.5)	
Number of subjects censored, n (%)	186 (49.9)	126 (68.5)	
Median time to first event (months) [a]	7.5	11.3	
95% Confidence Interval	[4.4, 10.4]	[8.6, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			1.5735
95% Confidence Interval			[1.1664, 2.1227]
p-value			0.0030
Stratified log-rank p-value [c]			0.0030

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Symptom Scales/Pain

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	128 (34.3)	80 (43.5)	
Number of subjects censored, n (%)	245 (65.7)	104 (56.5)	
Median time to first event (months) [a]	18.2	7.2	
95% Confidence Interval	[15.7, 23.0]	[4.7, 8.7]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.4265
95% Confidence Interval			[0.3168, 0.5743]
p-value			<0.0001
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Common Symptoms/Dyspnoea

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	122 (32.7)	47 (25.5)	
Number of subjects censored, n (%)	251 (67.3)	137 (74.5)	
Median time to first event (months) [a]	21.7	NE	
95% Confidence Interval	[15.9, NE]	[9.4, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.8744
95% Confidence Interval			[0.6197, 1.2339]
p-value			0.4449
Stratified log-rank p-value [c]			0.4410

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Common Symptoms/Insomnia

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	108 (29.0)	60 (32.6)	
Number of subjects censored, n (%)	265 (71.0)	124 (67.4)	
Median time to first event (months) [a]	NE	10.0	
95% Confidence Interval	[18.3, NE]	[6.9, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.5634
95% Confidence Interval			[0.4066, 0.7806]
p-value			0.0006
Stratified log-rank p-value [c]			0.0005

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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#### Common Symptoms/Appetite Loss

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	160 (42.9)	62 (33.7)	
Number of subjects censored, n (%)	213 (57.1)	122 (66.3)	
Median time to first event (months) [a]	13.6	11.3	
95% Confidence Interval	[10.4, 22.3]	[8.5, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.9955
95% Confidence Interval			[0.7385, 1.3417]
p-value			0.9762
Stratified log-rank p-value [c]			0.9563

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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#### Common Symptoms/Constipation

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	155 (41.6)	55 (29.9)	
Number of subjects censored, n (%)	218 (58.4)	129 (70.1)	
Median time to first event (months) [a]	13.6	11.3	
95% Confidence Interval	[10.1, NE]	[8.3, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			1.1670
95% Confidence Interval			[0.8537, 1.5952]
p-value			0.3330
Stratified log-rank p-value [c]			0.3382

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Common Symptoms/Diarrhea

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	101 (27.1)	36 (19.6)	
Number of subjects censored, n (%)	272 (72.9)	148 (80.4)	
Median time to first event (months) [a] 95% Confidence Interval	NE [21.7, NE]	NE [11.4, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.0605 [0.7202, 1.5617] 0.7659
Stratified log-rank p-value [c]			0.7750

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Common Symptoms/Financial Difficulties

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	79 (21.2)	42 (22.8)	
Number of subjects censored, n (%)	294 (78.8)	142 (77.2)	
Median time to first event (months) [a]	28.1	17.5	
95% Confidence Interval	[28.1, NE]	[11.3, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.5917
95% Confidence Interval			[0.4011, 0.8727]
p-value			0.0081
Stratified log-rank p-value [c]			0.0074

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.5025
HER2 IHC 1+	214	91 (42.5)	123 (57.5)	14.4 (8.8, 20.8)	107	48 (44.9)	59 (55.1)	6.9 (4.4, 9.9)	0.6362 (0.4453, 0.9090) 0.0130	0.0119	
HER2 IHC 2+/ISH Negative	159	69 (43.4)	90 (56.6)	15.7 (9.8, 18.6)	77	29 (37.7)	48 (62.3)	9.0 (5.9, NE)	0.7659 (0.4905, 1.1959) 0.2408	0.2379	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.2852
1	221	103 (46.6)	118 (53.4)	11.1 (8.8, 18.0)	100	40 (40.0)	60 (60.0)	9.0 (6.5, 11.4)	0.7685 (0.5287, 1.1170) 0.1675	0.1622
>=2	151	57 (37.7)	94 (62.3)	18.4 (11.3, NE)	83	37 (44.6)	46 (55.4)	6.9 (4.4, 9.9)	0.5935 (0.3891, 0.9052) 0.0154	0.0141

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Global Health Status

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.8112
Yes	235	105 (44.7)	130 (55.3)	11.3 (8.4, 18.2)	118	50 (42.4)	68 (57.6)	7.0 (4.4, 9.5)	0.6850 (0.4853, 0.9669) 0.0315	0.0299	
No	98	43 (43.9)	55 (56.1)	16.1 (9.8, 22.1)	48	20 (41.7)	28 (58.3)	11.4 (5.4, NE)	0.7119 (0.4133, 1.2264) 0.2208	0.2163	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Age										0.7419
<65	290	123 (42.4)	167 (57.6)	15.7 (9.8, 20.8)	136	53 (39.0)	83 (61.0)	8.4 (5.4, 11.4)	0.6744 (0.4846, 0.9385) 0.0195	0.0181
>=65	83	37 (44.6)	46 (55.4)	11.1 (5.9, 18.4)	48	24 (50.0)	24 (50.0)	7.5 (3.7, 13.6)	0.7581 (0.4504, 1.2759) 0.2971	0.2904

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8221
<75	359	154 (42.9)	205 (57.1)	14.4 (9.8, 18.4)	175	72 (41.1)	103 (58.9)	8.4 (5.9, 10.8)	0.6817 (0.5119, 0.9080) 0.0088	0.0080	
>=75	14	6 (42.9)	8 (57.1)	9.7 (4.2, NE)	9	5 (55.6)	4 (44.4)	9.9 (1.6, NE)	0.7418 (0.2255, 2.4400) 0.6230	0.6217	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Race										0.4526
White	176	67 (38.1)	109 (61.9)	18.6 (10.1, NE)	91	35 (38.5)	56 (61.5)	8.6 (4.2, 11.4)	0.6201 (0.4081, 0.9422) 0.0252	0.0237
Non-White	197	93 (47.2)	104 (52.8)	11.3 (8.4, 18.0)	92	42 (45.7)	50 (54.3)	7.0 (5.8, 11.4)	0.7281 (0.5012, 1.0576) 0.0958	0.0917

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.5515
Asia	147	80 (54.4)	67 (45.6)	9.7 (7.2, 15.7)	66	32 (48.5)	34 (51.5)	6.5 (3.8, NE)	0.8101 (0.5333, 1.2304) 0.3233	0.3172	
North America	60	21 (35.0)	39 (65.0)	22.3 (6.3, NE)	33	13 (39.4)	20 (60.6)	8.6 (2.0, NE)	0.5603 (0.2735, 1.1477) 0.1133	0.1098	
Europe + Israel	166	59 (35.5)	107 (64.5)	18.6 (11.4, NE)	85	32 (37.6)	53 (62.4)	9.0 (4.5, 15.3)	0.5953 (0.3834, 0.9242) 0.0208	0.0191	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]	
ECOG PS										0.7522	
0	200	94 (47.0)	106 (53.0)	13.1 (8.4, 18.4)	105	43 (41.0)	62 (59.0)	9.0 (5.3, 11.4)	0.7144 (0.4946, 1.0319)	0.0730	
1	173	66 (38.2)	107 (61.8)	16.1 (10.5, 22.3)	79	34 (43.0)	45 (57.0)	8.4 (4.5, 13.6)	0.6440 (0.4206, 0.9859)	0.0399	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.1501
0	60	25 (41.7)	35 (58.3)	9.7 (6.3, NE)	34	14 (41.2)	20 (58.8)	5.9 (4.5, NE)	0.6316 (0.3222, 1.2382) 0.1810	0.1759
1	108	43 (39.8)	65 (60.2)	16.3 (8.3, NE)	51	18 (35.3)	33 (64.7)	11.4 (9.0, NE)	1.0285 (0.5921, 1.7866) 0.9205	0.9212
2	115	45 (39.1)	70 (60.9)	22.3 (9.4, NE)	54	27 (50.0)	27 (50.0)	6.9 (2.9, 10.8)	0.4383 (0.2671, 0.7192) 0.0011	0.0008

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	47 (52.2)	43 (47.8)	11.4 (7.0, 18.4)	45	18 (40.0)	27 (60.0)	8.6 (3.1, NE)	0.7707 (0.4373, 1.3583) 0.3677	0.3642

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.6434
PD	174	62 (35.6)	112 (64.4)	18.0 (9.9, NE)	85	36 (42.4)	49 (57.6)	7.0 (5.3, 10.8)	0.5410 (0.3553, 0.8239) 0.0042	0.0036
PR	48	25 (52.1)	23 (47.9)	11.3 (8.1, 22.3)	22	8 (36.4)	14 (63.6)	3.9 (3.1, NE)	0.7276 (0.3198, 1.6554) 0.4483	0.4390
SD	82	38 (46.3)	44 (53.7)	14.4 (6.3, NE)	55	24 (43.6)	31 (56.4)	9.0 (4.5, 15.5)	0.7916 (0.4695, 1.3348) 0.3807	0.3754

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.7529
Yes	37	12 (32.4)	25 (67.6)	18.6 (8.8, NE)	15	3 (20.0)	12 (80.0)	NE (1.0, NE)	0.8346 (0.2281, 3.0531) 0.7846	0.7844	
No	336	148 (44.0)	188 (56.0)	13.1 (9.7, 18.2)	169	74 (43.8)	95 (56.2)	8.4 (5.8, 9.9)	0.6897 (0.5184, 0.9175) 0.0107	0.0099	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0052
Yes	24	12 (50.0)	12 (50.0)	9.9 (5.2, NE)	8	0	8 (100)	NE (NE, NE)	NE (NE, NE) 0.9942	0.1125	
No	349	148 (42.4)	201 (57.6)	14.4 (9.8, 18.4)	176	77 (43.8)	99 (56.3)	7.5 (5.4, 9.9)	0.6488 (0.4895, 0.8601) 0.0026	0.0023	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Renal function at baseline										0.0990
Normal Function	202	73 (36.1)	129 (63.9)	20.8 (15.7, NE)	87	35 (40.2)	52 (59.8)	6.9 (4.2, 13.6)	0.5589 (0.3684, 0.8479)	0.0062
Mild Impairment	123	68 (55.3)	55 (44.7)	8.4 (6.0, 11.3)	69	30 (43.5)	39 (56.5)	9.0 (3.8, 11.4)	0.8168 (0.5262, 1.2677)	0.3606
Moderate Impairment	41	17 (41.5)	24 (58.5)	16.3 (6.3, NE)	23	9 (39.1)	14 (60.9)	11.4 (5.9, NE)	1.1662 (0.5192, 2.6194)	0.7134

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.8366
Normal Function	170	76 (44.7)	94 (55.3)	16.1 (9.6, 22.3)	98	42 (42.9)	56 (57.1)	8.4 (5.8, 11.4)	0.7138 (0.4856, 1.0491) 0.0862	0.0821
Mild Impairment	195	82 (42.1)	113 (57.9)	13.1 (8.8, 18.6)	84	34 (40.5)	50 (59.5)	8.6 (4.2, 10.8)	0.6618 (0.4396, 0.9963) 0.0479	0.0454

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline visceral disease										0.8300
Yes	332	141 (42.5)	191 (57.5)	14.4 (9.9, 18.6)	157	63 (40.1)	94 (59.9)	9.3 (6.5, 11.4)	0.7010 (0.5176, 0.9494) 0.0217	0.0206
No	41	19 (46.3)	22 (53.7)	9.8 (4.2, NE)	27	14 (51.9)	13 (48.1)	5.8 (2.3, 9.0)	0.6497 (0.3189, 1.3234) 0.2348	0.2288

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (IXRS)										0.6740
Positive	331	147 (44.4)	184 (55.6)	13.2 (9.8, 18.4)	163	68 (41.7)	95 (58.3)	8.6 (5.9, 11.4)	0.7072 (0.5273, 0.9484)	0.0194
Negative	42	13 (31.0)	29 (69.0)	14.4 (8.4, NE)	21	9 (42.9)	12 (57.1)	5.8 (3.9, NE)	0.5127 (0.2103, 1.2502)	0.1354

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.9491
Positive	333	147 (44.1)	186 (55.9)	13.2 (9.8, 18.4)	166	70 (42.2)	96 (57.8)	8.4 (5.9, 11.4)	0.6964 (0.5206, 0.9315) 0.0148	0.0137	
Negative	40	13 (32.5)	27 (67.5)	14.4 (8.4, NE)	18	7 (38.9)	11 (61.1)	9.9 (3.2, NE)	0.5972 (0.2295, 1.5542) 0.2908	0.2861	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.3871
HER2 IHC 1+	214	83 (38.8)	131 (61.2)	16.6 (11.3, 21.7)	107	43 (40.2)	64 (59.8)	8.5 (4.9, 11.7)	0.5610 (0.3832, 0.8214) 0.0030	0.0026
HER2 IHC 2+/ISH Negative	159	57 (35.8)	102 (64.2)	NE (11.4, NE)	77	37 (48.1)	40 (51.9)	6.1 (3.9, 10.1)	0.4675 (0.3069, 0.7122) 0.0004	0.0003

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.3672
1	221	85 (38.5)	136 (61.5)	16.6 (11.3, 21.7)	100	41 (41.0)	59 (59.0)	8.1 (5.3, 10.5)	0.5706 (0.3892, 0.8365) 0.0040	0.0037
>=2	151	55 (36.4)	96 (63.6)	21.4 (11.3, NE)	83	39 (47.0)	44 (53.0)	5.9 (4.0, 9.8)	0.4622 (0.3032, 0.7046) 0.0003	0.0002

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Prior CDK4/6											
Yes	235	87 (37.0)	148 (63.0)	16.9 (11.3, 21.5)	118	48 (40.7)	70 (59.3)	8.1 (5.7, 10.1)	0.5377 (0.3736, 0.7738) 0.0008	0.0007	0.6556
No	98	39 (39.8)	59 (60.2)	21.7 (11.2, NE)	48	24 (50.0)	24 (50.0)	6.1 (3.9, 11.7)	0.4931 (0.2939, 0.8273) 0.0074	0.0063	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6857
<65	290	113 (39.0)	177 (61.0)	16.9 (11.3, 21.7)	136	58 (42.6)	78 (57.4)	6.8 (4.9, 9.8)	0.5290 (0.3818, 0.7331) 0.0001	<0.0001	
>=65	83	27 (32.5)	56 (67.5)	NE (11.4, NE)	48	22 (45.8)	26 (54.2)	9.5 (3.1, NE)	0.4632 (0.2609, 0.8223) 0.0086	0.0073	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7450
<75	359	137 (38.2)	222 (61.8)	16.9 (12.5, NE)	175	76 (43.4)	99 (56.6)	7.5 (5.3, 9.8)	0.5137 (0.3849, 0.6856) <0.0001	<0.0001	
>=75	14	3 (21.4)	11 (78.6)	NE (3.4, NE)	9	4 (44.4)	5 (55.6)	NE (0.7, NE)	0.4399 (0.0983, 1.9689) 0.2828	0.2694	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race									0.7695
White	176	61 (34.7)	115 (65.3) (11.3, NE)	91	34 (37.4)	57 (62.6) (4.5, 14.1)	0.5515 (0.3584, 0.8487) 0.0068	0.0061	
Non-White	197	79 (40.1)	118 (59.9) (11.2, NE)	92	46 (50.0)	46 (50.0) (4.2, 9.8)	0.4929 (0.3391, 0.7162) 0.0002	0.0002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.6195
Asia	147	67 (45.6)	80 (54.4)	16.3 (8.7, 21.7)	66	32 (48.5)	34 (51.5)	6.1 (4.6, 10.5)	0.5941 (0.3862, 0.9139) 0.0178	0.0165	
North America	60	17 (28.3)	43 (71.7)	21.5 (12.5, NE)	33	12 (36.4)	21 (63.6)	10.1 (1.6, NE)	0.4527 (0.2098, 0.9768) 0.0434	0.0388	
Europe + Israel	166	56 (33.7)	110 (66.3)	16.6 (11.4, NE)	85	36 (42.4)	49 (57.6)	7.5 (4.2, 10.2)	0.4924 (0.3207, 0.7560) 0.0012	0.0009	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	200	71 (35.5)	129 (64.5)	21.4 (13.2, NE)	105	42 (40.0)	63 (60.0)	8.1 (4.9, 14.1)	0.4733 (0.3202, 0.6997)	0.0001	0.5164
1	173	69 (39.9)	104 (60.1)	11.4 (9.2, NE)	79	38 (48.1)	41 (51.9)	6.8 (4.5, 9.8)	0.5722 (0.3796, 0.8625)	0.0069	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.9743
0	60	23 (38.3)	37 (61.7)	11.3 (6.9, NE)	34	14 (41.2)	20 (58.8)	5.3 (1.7, NE)	0.5223 (0.2650, 1.0295) 0.0607	0.0575
1	108	37 (34.3)	71 (65.7)	17.2 (11.3, NE)	51	23 (45.1)	28 (54.9)	9.5 (5.3, 14.1)	0.5843 (0.3461, 0.9862) 0.0442	0.0422
2	115	41 (35.7)	74 (64.3)	21.5 (12.5, NE)	54	22 (40.7)	32 (59.3)	7.5 (4.2, NE)	0.4590 (0.2644, 0.7968) 0.0057	0.0045

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%) Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%) Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	39 (43.3)	51 (56.7) 11.4 (8.7, NE)	45	21 (46.7)	24 (53.3) 7.7 (2.8, NE)	0.5012 (0.2877, 0.8731) 0.0147	0.0128	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.9871
PD	174	61 (35.1)	113 (64.9)	16.6 (11.4, NE)	85	35 (41.2)	50 (58.8)	7.5 (4.2, 9.5)	0.4683 (0.3041, 0.7210) 0.0006	0.0004	
PR	48	21 (43.8)	27 (56.3)	16.9 (8.7, NE)	22	9 (40.9)	13 (59.1)	11.7 (1.4, NE)	0.5385 (0.2396, 1.2102) 0.1341	0.1282	
SD	82	28 (34.1)	54 (65.9)	NE (11.3, NE)	55	24 (43.6)	31 (56.4)	8.4 (5.7, NE)	0.5310 (0.3033, 0.9296) 0.0267	0.0242	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.3852
Yes	37	18 (48.6)	19 (51.4)	7.1 (3.0, NE)	15	5 (33.3)	10 (66.7)	NE (0.8, NE)	0.8530 (0.3142, 2.3158)	0.7648
No	336	122 (36.3)	214 (63.7)	17.2 (13.1, NE)	169	75 (44.4)	94 (55.6)	7.5 (5.3, 9.8)	0.4793 (0.3562, 0.6449)	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.4603
Yes	24	12 (50.0)	12 (50.0)	9.6 (1.6, NE)	8	3 (37.5)	5 (62.5)	NE (0.7, NE)	0.8735 (0.2448, 3.1168)	0.8656	
No	349	128 (36.7)	221 (63.3)	17.2 (12.5, NE)	176	77 (43.8)	99 (56.3)	7.5 (5.3, 9.8)	0.4894 (0.3657, 0.6550)	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Renal function at baseline										0.0416
Normal Function	202	71 (35.1)	131 (64.9)	21.5 (11.3, NE)	87	42 (48.3)	45 (51.7)	4.9 (3.1, 8.5)	0.3900 (0.2624, 0.5796)	<0.0001
Mild Impairment	123	49 (39.8)	74 (60.2)	16.3 (9.0, NE)	69	28 (40.6)	41 (59.4)	7.5 (5.7, 11.7)	0.5308 (0.3264, 0.8632)	0.0094
Moderate Impairment	41	17 (41.5)	24 (58.5)	16.6 (9.1, NE)	23	8 (34.8)	15 (65.2)	NE (5.9, NE)	1.1796 (0.5079, 2.7400)	0.7014

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.4311
Normal Function	170	64 (37.6)	106 (62.4)	21.5 (12.5, NE)	98	46 (46.9)	52 (53.1)	6.8 (4.2, 11.7)	0.4696 (0.3187, 0.6921) 0.0001	<0.0001
Mild Impairment	195	74 (37.9)	121 (62.1)	17.2 (10.2, NE)	84	34 (40.5)	50 (59.5)	7.7 (4.9, 10.1)	0.5572 (0.3665, 0.8471) 0.0062	0.0055

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.0335
Yes	332	126 (38.0)	206 (62.0)	16.9 (12.5, 21.7)	157	64 (40.8)	93 (59.2)	8.4 (5.8, 10.2)	0.5875 (0.4320, 0.7988) 0.0007	0.0006	
No	41	14 (34.1)	27 (65.9)	NE (9.4, NE)	27	16 (59.3)	11 (40.7)	4.5 (1.4, 5.9)	0.2254 (0.1017, 0.4995) 0.0002	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)									0.5113
Positive	331	124 (37.5)	207 (62.5) (12.5, NE)	163	69 (42.3)	94 (57.7) (5.7, 10.1)	0.5271 (0.3897, 0.7129) <0.0001	<0.0001	
Negative	42	16 (38.1)	26 (61.9) (5.4, NE)	21	11 (52.4)	10 (47.6) (1.4, NE)	0.4721 (0.2133, 1.0448) 0.0641	0.0584	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Physical Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)									0.8259
Positive	333	125 (37.5)	208 (62.5) (12.5, NE)	166	72 (43.4)	94 (56.6) (5.3, 10.1)	0.5158 (0.3830, 0.6946) <0.0001	<0.0001	
Negative	40	15 (37.5)	25 (62.5) (5.4, NE)	18	8 (44.4)	10 (55.6) (0.8, NE)	0.5404 (0.2234, 1.3067) 0.1719	0.1674	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.9633
HER2 IHC 1+	214	94 (43.9)	120 (56.1)	11.3 (8.3, 21.5)	107	49 (45.8)	58 (54.2)	4.7 (4.2, 7.2)	0.5449 (0.3814, 0.7784) 0.0008	0.0007
HER2 IHC 2+/ISH Negative	159	65 (40.9)	94 (59.1)	16.8 (9.0, NE)	77	37 (48.1)	40 (51.9)	6.1 (2.9, 10.5)	0.5728 (0.3801, 0.8631) 0.0077	0.0068

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.6146
1	221	98 (44.3)	123 (55.7)	11.3 (7.2, 21.7)	100	48 (48.0)	52 (52.0)	5.8 (3.8, 7.7)	0.6082 (0.4287, 0.8629) 0.0053	0.0048	
>=2	151	61 (40.4)	90 (59.6)	16.6 (10.4, 27.2)	83	38 (45.8)	45 (54.2)	4.7 (2.9, 8.4)	0.5092 (0.3347, 0.7747) 0.0016	0.0013	

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.2241
Yes	235	98 (41.7)	137 (58.3)	16.4 (8.5, 23.0)	118	54 (45.8)	64 (54.2)	5.8 (3.7, 7.7)	0.5871 (0.4188, 0.8231) 0.0020	0.0017	
No	98	42 (42.9)	56 (57.1)	16.6 (10.4, NE)	48	27 (56.3)	21 (43.8)	4.3 (1.7, 8.4)	0.3722 (0.2255, 0.6144) 0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1712
<65	290	115 (39.7)	175 (60.3)	16.8 (11.3, 23.0)	136	62 (45.6)	74 (54.4)	5.8 (3.8, 7.7)	0.5069 (0.3693, 0.6958) <0.0001	<0.0001	
>=65	83	44 (53.0)	39 (47.0)	7.1 (4.4, 16.6)	48	24 (50.0)	24 (50.0)	4.8 (2.9, 10.5)	0.7916 (0.4779, 1.3114) 0.3643	0.3604	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2154
<75	359	152 (42.3)	207 (57.7)	16.4 (10.0, 21.5)	175	82 (46.9)	93 (53.1)	4.8 (4.2, 7.2)	0.5388 (0.4092, 0.7095) <0.0001	<0.0001	
>=75	14	7 (50.0)	7 (50.0)	9.7 (2.1, NE)	9	4 (44.4)	5 (55.6)	NE (0.8, NE)	1.2098 (0.3523, 4.1542) 0.7622	0.7726	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.2865
White	176	74 (42.0)	102 (58.0)	16.0 (8.5, 21.5)	91	37 (40.7)	54 (59.3)	6.7 (4.4, NE)	0.6895 (0.4613, 1.0308) 0.0699	0.0671	
Non-White	197	85 (43.1)	112 (56.9)	16.6 (8.7, 27.2)	92	49 (53.3)	43 (46.7)	4.7 (2.9, 7.1)	0.4730 (0.3299, 0.6783) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.5273
Asia	147	71 (48.3)	76 (51.7)	11.3 (7.5, 23.0)	66	38 (57.6)	28 (42.4)	4.7 (2.9, 7.0)	0.5005 (0.3347, 0.7486) 0.0008	0.0006	
North America	60	18 (30.0)	42 (70.0)	16.8 (7.3, NE)	33	13 (39.4)	20 (60.6)	4.5 (1.5, NE)	0.4281 (0.2014, 0.9098) 0.0274	0.0227	
Europe + Israel	166	70 (42.2)	96 (57.8)	16.0 (8.5, NE)	85	35 (41.2)	50 (58.8)	7.2 (4.4, NE)	0.7009 (0.4643, 1.0581) 0.0908	0.0883	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.1495
0	200	78 (39.0)	122 (61.0)	21.7 (12.0, NE)	105	48 (45.7)	57 (54.3)	4.7 (2.1, 8.4)	0.4736 (0.3278, 0.6841) 0.0001	<0.0001	
1	173	81 (46.8)	92 (53.2)	9.0 (6.7, 16.6)	79	38 (48.1)	41 (51.9)	6.1 (4.4, 8.4)	0.6724 (0.4527, 0.9986) 0.0492	0.0466	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.2965
0	60	30 (50.0)	30 (50.0)	9.7 (5.1, 17.6)	34	13 (38.2)	21 (61.8)	5.9 (2.9, NE)	0.7739 (0.3939, 1.5205) 0.4569	0.4546	
1	108	42 (38.9)	66 (61.1)	13.1 (9.6, NE)	51	21 (41.2)	30 (58.8)	7.2 (1.6, NE)	0.6629 (0.3906, 1.1251) 0.1277	0.1255	
2	115	40 (34.8)	75 (65.2)	21.5 (21.5, NE)	54	26 (48.1)	28 (51.9)	4.6 (2.1, 8.4)	0.4021 (0.2409, 0.6712) 0.0005	0.0003	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	47 (52.2)	43 (47.8)	8.3 (6.0, 16.4)	45	26 (57.8)	19 (42.2)	4.2 (1.5, 7.7)	0.5275 (0.3218, 0.8647) 0.0112	0.0099

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.8344
PD	174	63 (36.2)	111 (63.8)	27.2 (8.5, NE)	85	34 (40.0)	51 (60.0)	7.0 (3.7, NE)	0.6111 (0.4000, 0.9336) 0.0227	0.0213	
PR	48	25 (52.1)	23 (47.9)	11.3 (7.0, 21.5)	22	9 (40.9)	13 (59.1)	8.4 (0.9, NE)	0.6322 (0.2880, 1.3876) 0.2529	0.2443	
SD	82	37 (45.1)	45 (54.9)	16.6 (8.3, NE)	55	28 (50.9)	27 (49.1)	4.7 (3.8, 7.2)	0.5554 (0.3355, 0.9195) 0.0222	0.0205	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.7007
Yes	37	13 (35.1)	24 (64.9)	16.6 (6.7, NE)	15	4 (26.7)	11 (73.3)	NE (1.0, NE)	0.7945 (0.2539, 2.4864) 0.6927	0.6910	
No	336	146 (43.5)	190 (56.5)	13.1 (9.6, 21.5)	169	82 (48.5)	87 (51.5)	4.8 (4.2, 7.2)	0.5555 (0.4212, 0.7325) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0998
Yes	24	10 (41.7)	14 (58.3)	16.6 (4.9, NE)	8	1 (12.5)	7 (87.5)	NE (0.7, NE)	2.4679 (0.3113, 19.5677) 0.3925	0.3730	
No	349	149 (42.7)	200 (57.3)	16.0 (9.8, 21.5)	176	85 (48.3)	91 (51.7)	4.8 (3.8, 7.1)	0.5419 (0.4125, 0.7118) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0098
Normal Function	202	76 (37.6)	126 (62.4)	16.6 (12.0, NE)	87	42 (48.3)	45 (51.7)	4.3 (1.5, 8.6)	0.4147 (0.2811, 0.6120) <0.0001	<0.0001	
Mild Impairment	123	59 (48.0)	64 (52.0)	9.7 (6.7, 23.0)	69	33 (47.8)	36 (52.2)	5.8 (4.2, 8.4)	0.6300 (0.4062, 0.9772) 0.0391	0.0368	
Moderate Impairment	41	22 (53.7)	19 (46.3)	7.0 (2.8, NE)	23	8 (34.8)	15 (65.2)	NE (4.5, NE)	1.5143 (0.6732, 3.4064) 0.3157	0.3096	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.6312
Normal Function	170	79 (46.5)	91 (53.5)	16.0 (7.7, 21.5)	98	47 (48.0)	51 (52.0)	5.9 (3.7, 8.6)	0.6123 (0.4241, 0.8840) 0.0088	0.0079	
Mild Impairment	195	78 (40.0)	117 (60.0)	16.6 (8.7, 23.0)	84	38 (45.2)	46 (54.8)	4.8 (2.9, 8.4)	0.5175 (0.3472, 0.7712) 0.0012	0.0010	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.7371
Yes	332	140 (42.2)	192 (57.8)	16.0 (9.8, 21.5)	157	75 (47.8)	82 (52.2)	4.8 (3.8, 7.7)	0.5503 (0.4134, 0.7324) <0.0001	<0.0001	
No	41	19 (46.3)	22 (53.7)	11.3 (5.1, NE)	27	11 (40.7)	16 (59.3)	5.9 (1.7, NE)	0.6754 (0.3130, 1.4575) 0.3173	0.3078	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.1966
Positive	331	138 (41.7)	193 (58.3)	16.4 (10.4, 21.7)	163	77 (47.2)	86 (52.8)	5.8 (4.2, 7.7)	0.5247 (0.3946, 0.6978)	<0.0001	
Negative	42	21 (50.0)	21 (50.0)	6.0 (2.9, 17.6)	21	9 (42.9)	12 (57.1)	5.9 (1.5, NE)	0.9633 (0.4334, 2.1410)	0.9223	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Role Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.0241
Positive	333	139 (41.7)	194 (58.3)	16.4 (10.0, 21.7)	166	81 (48.8)	85 (51.2)	4.7 (3.7, 7.1)	0.5074 (0.3834, 0.6715) <0.0001	<0.0001	
Negative	40	20 (50.0)	20 (50.0)	6.0 (2.9, 17.6)	18	5 (27.8)	13 (72.2)	NE (3.4, NE)	1.5391 (0.5688, 4.1648) 0.3959	0.3951	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.9072
HER2 IHC 1+	214	73 (34.1)	141 (65.9)	19.2 (13.6, NE)	107	29 (27.1)	78 (72.9)	11.1 (7.1, NE)	0.7230 (0.4623, 1.1306)	0.1523
HER2 IHC 2+/ISH Negative	159	47 (29.6)	112 (70.4)	21.7 (18.7, NE)	77	20 (26.0)	57 (74.0)	NE (6.3, NE)	0.7636 (0.4488, 1.2995)	0.3190

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.1975
1	221	77 (34.8)	144 (65.2)	21.7 (16.3, NE)	100	26 (26.0)	74 (74.0)	11.1 (7.7, NE)	0.9245 (0.5876, 1.4545)	0.7312
>=2	151	43 (28.5)	108 (71.5)	NE (16.6, NE)	83	23 (27.7)	60 (72.3)	11.7 (6.1, NE)	0.5411 (0.3197, 0.9159)	0.0205

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6									0.2212
Yes	235	74 (31.5)	161 (68.5) (16.7, NE)	118	25 (21.2)	93 (78.8) (10.2, NE)	0.9088 (0.5712, 1.4460) 0.6866	0.6842	
No	98	35 (35.7)	63 (64.3) (13.1, NE)	48	18 (37.5)	30 (62.5) (5.9, NE)	0.5931 (0.3318, 1.0603) 0.0780	0.0746	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4814
<65	290	94 (32.4)	196 (67.6)	22.3 (19.2, NE)	136	33 (24.3)	103 (75.7)	NE (7.1, NE)	0.8109 (0.5401, 1.2177) 0.3123	0.3092	
>=65	83	26 (31.3)	57 (68.7)	17.0 (13.8, NE)	48	16 (33.3)	32 (66.7)	11.7 (7.7, NE)	0.5855 (0.3057, 1.1212) 0.1064	0.1028	

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5199
<75	359	116 (32.3)	243 (67.7)	21.7 (17.0, NE)	175	47 (26.9)	128 (73.1)	11.7 (7.7, NE)	0.7332 (0.5177, 1.0384) 0.0805	0.0786	
>=75	14	4 (28.6)	10 (71.4)	16.7 (8.5, NE)	9	2 (22.2)	7 (77.8)	NE (3.7, NE)	1.0547 (0.1756, 6.3355) 0.9536	0.9533	

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Race										0.7436
White	176	54 (30.7)	122 (69.3)	21.7 (16.7, NE)	91	21 (23.1)	70 (76.9)	11.1 (8.4, NE)	0.7841 (0.4655, 1.3207) 0.3606	0.3606
Non-White	197	66 (33.5)	131 (66.5)	22.8 (16.3, NE)	92	28 (30.4)	64 (69.6)	11.7 (6.9, NE)	0.7095 (0.4515, 1.1148) 0.1366	0.1351

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.7171
Asia	147	51 (34.7)	96 (65.3)	22.8 (13.6, NE)	66	19 (28.8)	47 (71.2)	NE (6.9, NE)	0.7913 (0.4626, 1.3536) 0.3928	0.3928	
North America	60	15 (25.0)	45 (75.0)	22.3 (19.2, NE)	33	8 (24.2)	25 (75.8)	NE (4.4, NE)	0.6281 (0.2551, 1.5467) 0.3118	0.3078	
Europe + Israel	166	54 (32.5)	112 (67.5)	21.7 (13.8, NE)	85	22 (25.9)	63 (74.1)	11.1 (8.4, NE)	0.7714 (0.4638, 1.2829) 0.3172	0.3163	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
ECOG PS										0.8101
0	200	65 (32.5)	135 (67.5)	22.8 (16.7, NE)	105	25 (23.8)	80 (76.2)	NE (11.1, NE)	0.7848 (0.4902, 1.2562) 0.3126	0.3118
1	173	55 (31.8)	118 (68.2)	18.7 (13.6, NE)	79	24 (30.4)	55 (69.6)	10.2 (6.9, NE)	0.6977 (0.4235, 1.1493) 0.1575	0.1540

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.0714
0	60	19 (31.7)	41 (68.3)	18.7 (10.4, NE)	34	9 (26.5)	25 (73.5)	7.1 (5.3, NE)	0.7737 (0.3433, 1.7437) 0.5360	0.5385	
1	108	39 (36.1)	69 (63.9)	17.0 (11.1, 22.8)	51	12 (23.5)	39 (76.5)	NE (10.2, NE)	1.2270 (0.6376, 2.3613) 0.5402	0.5376	
2	115	37 (32.2)	78 (67.8)	22.3 (16.7, NE)	54	20 (37.0)	34 (63.0)	6.9 (4.2, NE)	0.4327 (0.2413, 0.7760) 0.0049	0.0038	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	25 (27.8)	65 (72.2)	NE (16.3, NE)	45	8 (17.8)	37 (82.2)	NE (NE, NE)	0.9767 (0.4336, 2.2005) 0.9547	0.9555

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.7697
PD	174	52 (29.9)	122 (70.1)	22.8 (16.3, NE)	85	23 (27.1)	62 (72.9)	NE (6.3, NE)	0.6463 (0.3889, 1.0741) 0.0921	0.0892	
PR	48	16 (33.3)	32 (66.7)	22.3 (11.2, NE)	22	4 (18.2)	18 (81.8)	11.7 (11.7, NE)	0.9784 (0.3178, 3.0119) 0.9696	0.9766	
SD	82	25 (30.5)	57 (69.5)	19.2 (12.0, NE)	55	16 (29.1)	39 (70.9)	11.1 (8.4, NE)	0.7165 (0.3773, 1.3607) 0.3083	0.3061	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.9723
Yes	37	12 (32.4)	25 (67.6)	18.7 (9.7, NE)	15	3 (20.0)	12 (80.0)	NE (5.9, NE)	0.6381 (0.1693, 2.4054) 0.5070	0.5036	
No	336	108 (32.1)	228 (67.9)	22.3 (16.7, NE)	169	46 (27.2)	123 (72.8)	11.7 (8.4, NE)	0.7532 (0.5286, 1.0732) 0.1166	0.1143	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.2012
Yes	24	9 (37.5)	15 (62.5)	18.7 (7.1, NE)	8	1 (12.5)	7 (87.5)	NE (5.9, NE)	2.0152 (0.2486, 16.3377)	0.5032
No	349	111 (31.8)	238 (68.2)	21.7 (16.7, NE)	176	48 (27.3)	128 (72.7)	11.7 (8.4, NE)	0.7130 (0.5035, 1.0097)	0.0552

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline									0.0463
Normal Function	202	70 (34.7)	132 (65.3) (13.6, NE)	87	18 (20.7)	69 (79.3) (6.9, NE)	1.0839 (0.6399, 1.8359) 0.7645	0.7664	
Mild Impairment	123	35 (28.5)	88 (71.5) (16.3, NE)	69	24 (34.8)	45 (65.2) (5.7, 11.7)	0.4078 (0.2343, 0.7100) 0.0015	0.0011	
Moderate Impairment	41	15 (36.6)	26 (63.4) (11.2, NE)	23	7 (30.4)	16 (69.6) (7.7, NE)	1.0453 (0.4245, 2.5740) 0.9232	0.9226	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline									0.0663
Normal Function	170	56 (32.9)	114 (67.1) (17.0, NE)	98	34 (34.7)	64 (65.3) (6.3, NE)	0.5794 (0.3736, 0.8987) 0.0148	0.0136	
Mild Impairment	195	64 (32.8)	131 (67.2) (13.1, NE)	84	15 (17.9)	69 (82.1) (10.2, NE)	1.1061 (0.6232, 1.9632) 0.7306	0.7315	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline visceral disease										0.0254
Yes	332	108 (32.5)	224 (67.5)	21.7 (16.6, NE)	157	37 (23.6)	120 (76.4)	NE (10.2, NE)	0.8715 (0.5954, 1.2756) 0.4791	0.4778
No	41	12 (29.3)	29 (70.7)	NE (13.6, NE)	27	12 (44.4)	15 (55.6)	5.7 (3.7, NE)	0.3790 (0.1604, 0.8953) 0.0270	0.0218

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.3659
Positive	331	109 (32.9)	222 (67.1)	21.7 (16.7, NE)	163	42 (25.8)	121 (74.2)	11.7 (8.4, NE)	0.7863 (0.5463, 1.1319) 0.1959	0.1934	
Negative	42	11 (26.2)	31 (73.8)	18.7 (12.5, NE)	21	7 (33.3)	14 (66.7)	NE (3.4, NE)	0.5484 (0.2019, 1.4895) 0.2386	0.2323	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Emotional Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.5668
Positive	333	108 (32.4)	225 (67.6)	21.7 (16.7, NE)	166	43 (25.9)	123 (74.1)	11.7 (8.4, NE)	0.7654 (0.5329, 1.0994) 0.1480	0.1456	
Negative	40	12 (30.0)	28 (70.0)	18.7 (8.5, NE)	18	6 (33.3)	12 (66.7)	NE (3.0, NE)	0.6357 (0.2294, 1.7617) 0.3837	0.3785	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.5104
HER2 IHC 1+	214	86 (40.2)	128 (59.8)	17.0 (9.9, 21.4)	107	48 (44.9)	59 (55.1)	6.9 (4.4, 9.1)	0.5615 (0.3904, 0.8077) 0.0019	0.0016	
HER2 IHC 2+/ISH Negative	159	71 (44.7)	88 (55.3)	13.1 (9.2, 18.7)	77	34 (44.2)	43 (55.8)	8.5 (4.2, 16.2)	0.6996 (0.4624, 1.0584) 0.0908	0.0880	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.4704
1	221	96 (43.4)	125 (56.6)	12.7 (8.8, 17.3)	100	46 (46.0)	54 (54.0)	7.9 (4.2, 11.3)	0.6829 (0.4779, 0.9760) 0.0363	0.0348
>=2	151	61 (40.4)	90 (59.6)	16.0 (9.9, 21.4)	83	36 (43.4)	47 (56.6)	6.1 (4.4, 8.6)	0.5176 (0.3381, 0.7924) 0.0024	0.0021

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Prior CDK4/6										0.4976
Yes	235	95 (40.4)	140 (59.6)	13.6 (10.1, 17.3)	118	53 (44.9)	65 (55.1)	6.0 (4.2, 8.6)	0.5675 (0.4025, 0.8003) 0.0012	0.0010
No	98	46 (46.9)	52 (53.1)	16.0 (7.5, NE)	48	21 (43.8)	27 (56.3)	11.1 (4.2, 16.2)	0.7389 (0.4377, 1.2474) 0.2574	0.2561

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Age										0.9204
<65	290	123 (42.4)	167 (57.6)	13.1 (9.9, 21.4)	136	59 (43.4)	77 (56.6)	6.5 (4.4, 8.6)	0.6035 (0.4392, 0.8293) 0.0018	0.0016
>=65	83	34 (41.0)	49 (59.0)	13.8 (8.3, NE)	48	23 (47.9)	25 (52.1)	9.1 (3.1, 11.7)	0.6009 (0.3489, 1.0352) 0.0664	0.0654

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5396
<75	359	151 (42.1)	208 (57.9)	13.6 (10.4, 17.6)	175	77 (44.0)	98 (56.0)	6.5 (4.4, 9.0)	0.6047 (0.4567, 0.8005) 0.0004	0.0004	
>=75	14	6 (42.9)	8 (57.1)	14.1 (2.9, NE)	9	5 (55.6)	4 (44.4)	11.1 (2.8, NE)	0.6927 (0.1979, 2.4240) 0.5656	0.5635	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Race										0.3360
White	176	69 (39.2)	107 (60.8)	13.8 (10.4, 18.7)	91	40 (44.0)	51 (56.0)	6.9 (3.9, 11.1)	0.5115 (0.3427, 0.7634) 0.0010	0.0008
Non-White	197	88 (44.7)	109 (55.3)	13.1 (7.6, 21.4)	92	42 (45.7)	50 (54.3)	8.5 (5.8, 9.1)	0.7097 (0.4885, 1.0310) 0.0719	0.0699

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Region										0.2376
Asia	147	74 (50.3)	73 (49.7)	11.8 (7.0, 17.5)	66	34 (51.5)	32 (48.5)	6.5 (5.8, 9.1)	0.7150 (0.4738, 1.0788) 0.1099	0.1084
North America	60	21 (35.0)	39 (65.0)	11.2 (7.1, NE)	33	7 (21.2)	26 (78.8)	7.9 (4.4, NE)	0.9792 (0.4046, 2.3703) 0.9629	0.9613
Europe + Israel	166	62 (37.3)	104 (62.7)	16.0 (11.8, NE)	85	41 (48.2)	44 (51.8)	5.4 (3.2, 11.1)	0.4819 (0.3215, 0.7225) 0.0004	0.0003

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	200	85 (42.5)	115 (57.5)	16.7 (11.8, 18.7)	105	43 (41.0)	62 (59.0)	7.9 (5.8, 11.7)	0.6466 (0.4455, 0.9384) 0.0218	0.0208	0.6458
1	173	72 (41.6)	101 (58.4)	11.3 (8.8, 22.3)	79	39 (49.4)	40 (50.6)	6.1 (4.2, 8.6)	0.5715 (0.3821, 0.8549) 0.0065	0.0058	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.7158
0	60	30 (50.0)	30 (50.0)	8.8 (3.9, 17.6)	34	16 (47.1)	18 (52.9)	5.9 (3.1, NE)	0.6758 (0.3621, 1.2614) 0.2185	0.2161
1	108	43 (39.8)	65 (60.2)	13.1 (7.6, NE)	51	23 (45.1)	28 (54.9)	9.0 (4.3, 17.1)	0.7516 (0.4520, 1.2498) 0.2711	0.2681
2	115	48 (41.7)	67 (58.3)	16.7 (11.8, 22.3)	54	22 (40.7)	32 (59.3)	7.9 (3.5, NE)	0.4746 (0.2755, 0.8178) 0.0073	0.0059

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	36 (40.0)	21.4 (7.1, NE)	45	21 (46.7)	6.5 (3.2, 9.1)	0.5854 (0.3391, 1.0106) 0.0546	0.0517	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.1580
PD	174	69 (39.7)	105 (60.3)	13.6 (9.2, 18.7)	85	33 (38.8)	52 (61.2)	6.9 (4.2, NE)	0.6350 (0.4144, 0.9730) 0.0370	0.0353
PR	48	20 (41.7)	28 (58.3)	22.3 (5.7, NE)	22	14 (63.6)	8 (36.4)	3.9 (2.8, 9.0)	0.3486 (0.1723, 0.7053) 0.0034	0.0021
SD	82	41 (50.0)	41 (50.0)	9.2 (6.9, 17.6)	55	26 (47.3)	29 (52.7)	9.0 (5.4, 16.2)	0.8188 (0.4972, 1.3485) 0.4323	0.4351

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.4675
Yes	37	15 (40.5)	22 (59.5)	11.8 (7.1, NE)	15	4 (26.7)	11 (73.3)	8.5 (6.0, NE)	0.8570 (0.2790, 2.6321) 0.7875	0.7873	
No	336	142 (42.3)	194 (57.7)	13.8 (10.4, 17.5)	169	78 (46.2)	91 (53.8)	6.5 (4.4, 9.0)	0.6025 (0.4544, 0.7990) 0.0004	0.0004	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0981
Yes	24	13 (54.2)	11 (45.8)	8.8 (4.2, NE)	8	2 (25.0)	6 (75.0)	12.8 (8.5, NE)	1.6826 (0.3736, 7.5782) 0.4980	0.4933	
No	349	144 (41.3)	205 (58.7)	14.1 (11.3, 17.6)	176	80 (45.5)	96 (54.5)	6.5 (4.4, 9.0)	0.5850 (0.4425, 0.7735) 0.0002	0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%) Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%) Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline									0.2373
Normal Function	202	80 (39.6)	122 (60.4) 22.3 (10.1, NE)	87	40 (46.0)	47 (54.0) 5.3 (3.5, 16.2)	0.5465 (0.3710, 0.8051) 0.0022	0.0019	
Mild Impairment	123	58 (47.2)	65 (52.8) 13.1 (7.1, 17.3)	69	32 (46.4)	37 (53.6) 6.5 (4.2, 9.0)	0.5473 (0.3474, 0.8623) 0.0094	0.0085	
Moderate Impairment	41	18 (43.9)	23 (56.1) 16.7 (5.6, NE)	23	9 (39.1)	14 (60.9) 17.1 (5.9, NE)	1.0308 (0.4586, 2.3168) 0.9415	0.9423	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Cognitive Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.9916
Normal Function	170	72 (42.4)	98 (57.6)	16.0 (10.1, NE)	98	45 (45.9)	53 (54.1)	8.5 (5.8, 11.1)	0.5949 (0.4072, 0.8692) 0.0073	0.0067
Mild Impairment	195	84 (43.1)	111 (56.9)	12.5 (9.2, 17.6)	84	37 (44.0)	47 (56.0)	6.0 (3.5, 11.3)	0.6101 (0.4099, 0.9081) 0.0149	0.0137

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.2324
Yes	332	140 (42.2)	192 (57.8)	13.6 (9.9, 17.6)	157	67 (42.7)	90 (57.3)	7.9 (5.8, 11.1)	0.6547 (0.4869, 0.8805) 0.0051	0.0048	
No	41	17 (41.5)	24 (58.5)	16.7 (5.7, NE)	27	15 (55.6)	12 (44.4)	4.4 (2.8, 9.0)	0.4040 (0.1930, 0.8458) 0.0162	0.0129	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (IXRS)										0.9708
Positive	331	138 (41.7)	193 (58.3)	13.8 (11.2, 17.5)	163	71 (43.6)	92 (56.4)	7.9 (5.4, 11.1)	0.6148 (0.4593, 0.8229) 0.0011	0.0010
Negative	42	19 (45.2)	23 (54.8)	8.8 (2.9, NE)	21	11 (52.4)	10 (47.6)	5.3 (3.9, 9.0)	0.6246 (0.2865, 1.3615) 0.2365	0.2328

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.8648
Positive	333	140 (42.0)	193 (58.0)	13.8 (10.8, 17.5)	166	74 (44.6)	92 (55.4)	7.7 (4.4, 9.1)	0.6107 (0.4583, 0.8138) 0.0008	0.0007	
Negative	40	17 (42.5)	23 (57.5)	11.8 (2.9, NE)	18	8 (44.4)	10 (55.6)	5.9 (4.4, 9.0)	0.6330 (0.2633, 1.5220) 0.3070	0.3006	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.1614
HER2 IHC 1+	214	91 (42.5)	123 (57.5)	12.8 (10.4, 21.5)	107	56 (52.3)	51 (47.7)	5.4 (3.5, 7.9)	0.4665 (0.3292, 0.6611) <0.0001	<0.0001	
HER2 IHC 2+/ISH Negative	159	65 (40.9)	94 (59.1)	14.3 (12.5, 21.7)	77	32 (41.6)	45 (58.4)	6.1 (4.6, NE)	0.7361 (0.4792, 1.1308) 0.1619	0.1554	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.1727
1	221	102 (46.2)	119 (53.8)	12.7 (8.3, 15.2)	100	48 (48.0)	52 (52.0)	6.0 (4.2, 9.7)	0.6830 (0.4818, 0.9683) 0.0323	0.0312	
>=2	151	54 (35.8)	97 (64.2)	17.5 (12.5, 23.0)	83	40 (48.2)	43 (51.8)	5.9 (4.4, 8.5)	0.4256 (0.2770, 0.6538) 0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.7051
Yes	235	94 (40.0)	141 (60.0)	13.6 (10.8, 21.5)	118	56 (47.5)	62 (52.5)	5.8 (4.3, 8.5)	0.5543 (0.3953, 0.7774) 0.0006	0.0005	
No	98	49 (50.0)	49 (50.0)	13.8 (9.1, 21.7)	48	23 (47.9)	25 (52.1)	7.1 (4.2, 9.7)	0.6218 (0.3716, 1.0404) 0.0704	0.0679	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0594
<65	290	118 (40.7)	172 (59.3)	14.6 (12.5, 21.5)	136	67 (49.3)	69 (50.7)	5.3 (4.2, 6.2)	0.4966 (0.3648, 0.6762) <0.0001	<0.0001	
>=65	83	38 (45.8)	45 (54.2)	10.8 (5.9, 19.3)	48	21 (43.8)	27 (56.3)	9.7 (4.7, NE)	0.8481 (0.4894, 1.4695) 0.5568	0.5516	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0349
<75	359	150 (41.8)	209 (58.2)	13.8 (11.3, 19.3)	175	86 (49.1)	89 (50.9)	5.4 (4.4, 7.0)	0.5309 (0.4038, 0.6979) <0.0001	<0.0001	
>=75	14	6 (42.9)	8 (57.1)	10.8 (2.8, NE)	9	2 (22.2)	7 (77.8)	11.3 (9.7, NE)	2.6548 (0.5324, 13.2387) 0.2337	0.2158	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.3539
White	176	71 (40.3)	105 (59.7)	13.6 (11.1, 21.7)	91	45 (49.5)	46 (50.5)	5.3 (2.8, 7.9)	0.5125 (0.3485, 0.7535) 0.0007	0.0005	
Non-White	197	85 (43.1)	112 (56.9)	13.1 (10.0, 19.3)	92	43 (46.7)	49 (53.3)	6.1 (4.6, 9.7)	0.6129 (0.4204, 0.8934) 0.0109	0.0099	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.5462
Asia	147	70 (47.6)	77 (52.4)	13.1 (9.2, 19.3)	66	32 (48.5)	34 (51.5)	7.0 (4.6, 11.3)	0.6466 (0.4215, 0.9918) 0.0458	0.0432	
North America	60	20 (33.3)	40 (66.7)	14.6 (10.4, NE)	33	13 (39.4)	20 (60.6)	5.8 (2.0, NE)	0.5465 (0.2611, 1.1440) 0.1089	0.1028	
Europe + Israel	166	66 (39.8)	100 (60.2)	13.6 (11.1, 23.0)	85	43 (50.6)	42 (49.4)	5.3 (2.9, 9.7)	0.5096 (0.3432, 0.7567) 0.0008	0.0006	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.3522
0	200	80 (40.0)	120 (60.0)	18.2 (12.5, 21.7)	105	49 (46.7)	56 (53.3)	5.4 (3.8, 9.7)	0.5040 (0.3498, 0.7262) 0.0002	0.0002	
1	173	76 (43.9)	97 (56.1)	12.8 (9.0, 14.6)	79	39 (49.4)	40 (50.6)	6.2 (4.4, 8.5)	0.6361 (0.4262, 0.9494) 0.0268	0.0244	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1099
0	60	26 (43.3)	34 (56.7)	11.3 (6.8, NE)	34	17 (50.0)	17 (50.0)	5.4 (3.4, 7.0)	0.5067 (0.2672, 0.9612) 0.0374	0.0340	
1	108	44 (40.7)	64 (59.3)	13.6 (9.0, 21.7)	51	24 (47.1)	27 (52.9)	8.5 (4.3, NE)	0.6647 (0.4014, 1.1005) 0.1124	0.1103	
2	115	45 (39.1)	70 (60.9)	18.2 (12.5, NE)	54	30 (55.6)	24 (44.4)	4.4 (2.0, 7.9)	0.3643 (0.2221, 0.5975) 0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	41 (45.6)	49 (54.4)	12.8 (9.1, 23.0)	45	17 (37.8)	28 (62.2)	7.7 (4.2, NE)	0.8403 (0.4695, 1.5038) 0.5579	0.5420

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.8604
PD	174	65 (37.4)	109 (62.6)	13.6 (10.8, 21.5)	85	39 (45.9)	46 (54.1)	5.8 (4.6, 8.5)	0.5246 (0.3469, 0.7933) 0.0022	0.0018	
PR	48	24 (50.0)	24 (50.0)	13.2 (4.2, NE)	22	10 (45.5)	12 (54.5)	5.7 (1.0, NE)	0.6093 (0.2871, 1.2929) 0.1968	0.1939	
SD	82	29 (35.4)	53 (64.6)	21.7 (12.7, NE)	55	28 (50.9)	27 (49.1)	6.1 (4.4, 11.3)	0.4678 (0.2736, 0.7999) 0.0055	0.0046	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.0463
Yes	37	17 (45.9)	20 (54.1)	11.2 (1.6, NE)	15	3 (20.0)	12 (80.0)	NE (2.1, NE)	1.9817 (0.5785, 6.7891) 0.2763	0.2706	
No	336	139 (41.4)	197 (58.6)	13.8 (11.3, 18.2)	169	85 (50.3)	84 (49.7)	5.8 (4.4, 7.7)	0.5129 (0.3882, 0.6778) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.0059
Yes	24	13 (54.2)	11 (45.8)	3.0 (0.9, NE)	8	1 (12.5)	7 (87.5)	NE (4.7, NE)	4.9290 (0.6415, 37.8736)	0.0893
No	349	143 (41.0)	206 (59.0)	13.8 (12.5, 19.3)	176	87 (49.4)	89 (50.6)	5.9 (4.4, 7.7)	0.5107 (0.3878, 0.6724)	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0376
Normal Function	202	83 (41.1)	119 (58.9)	15.2 (10.4, 21.7)	87	48 (55.2)	39 (44.8)	4.4 (2.9, 5.4)	0.4422 (0.3065, 0.6380) <0.0001	<0.0001	
Mild Impairment	123	54 (43.9)	69 (56.1)	13.1 (10.8, 19.3)	69	30 (43.5)	39 (56.5)	6.1 (4.2, NE)	0.5537 (0.3435, 0.8924) 0.0152	0.0133	
Moderate Impairment	41	17 (41.5)	24 (58.5)	13.6 (6.8, NE)	23	8 (34.8)	15 (65.2)	18.5 (7.0, NE)	1.2253 (0.5266, 2.8512) 0.6372	0.6357	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.8617
Normal Function	170	71 (41.8)	99 (58.2)	13.8 (11.3, NE)	98	46 (46.9)	52 (53.1)	6.1 (5.4, 9.7)	0.5917 (0.4041, 0.8663) 0.0070	0.0062	
Mild Impairment	195	84 (43.1)	111 (56.9)	13.1 (10.3, 18.2)	84	42 (50.0)	42 (50.0)	4.7 (2.9, 8.5)	0.5149 (0.3509, 0.7555) 0.0007	0.0005	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.3119
Yes	332	138 (41.6)	194 (58.4)	13.6 (11.2, 19.3)	157	72 (45.9)	85 (54.1)	6.2 (4.7, 8.5)	0.5915 (0.4418, 0.7919) 0.0004	0.0003	
No	41	18 (43.9)	23 (56.1)	17.5 (5.6, NE)	27	16 (59.3)	11 (40.7)	4.6 (1.5, 7.0)	0.4761 (0.2319, 0.9775) 0.0432	0.0368	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.7465
Positive	331	140 (42.3)	191 (57.7)	13.6 (11.3, 18.2)	163	76 (46.6)	87 (53.4)	6.1 (4.6, 8.5)	0.5703 (0.4281, 0.7599) 0.0001	<0.0001	
Negative	42	16 (38.1)	26 (61.9)	NE (4.7, NE)	21	12 (57.1)	9 (42.9)	4.4 (1.7, 7.0)	0.5999 (0.2784, 1.2928) 0.1921	0.1892	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Social Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.8301
Positive	333	142 (42.6)	191 (57.4)	13.6 (11.2, 18.2)	166	79 (47.6)	87 (52.4)	6.0 (4.6, 8.4)	0.5695 (0.4291, 0.7557) 0.0001	<0.0001	
Negative	40	14 (35.0)	26 (65.0)	NE (4.7, NE)	18	9 (50.0)	9 (50.0)	5.3 (1.7, NE)	0.5730 (0.2429, 1.3514) 0.2034	0.1966	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
HER2 status											0.5077
HER2 IHC 1+	214	97 (45.3)	117 (54.7)	11.2 (7.9, 17.6)	107	51 (47.7)	56 (52.3)	4.4 (2.9, 7.7)	0.5895 (0.4161, 0.8350) 0.0029	0.0027	
HER2 IHC 2+/ISH Negative	159	81 (50.9)	78 (49.1)	11.4 (7.1, 13.2)	77	41 (53.2)	36 (46.8)	5.9 (3.1, 8.1)	0.6947 (0.4743, 1.0175) 0.0613	0.0587	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.5540
1	221	109 (49.3)	112 (50.7)	9.8 (5.9, 13.6)	100	55 (55.0)	45 (45.0)	4.9 (1.9, 7.7)	0.6109 (0.4390, 0.8502) 0.0035	0.0032
>=2	151	69 (45.7)	82 (54.3)	11.8 (7.7, 16.1)	83	37 (44.6)	46 (55.4)	5.3 (3.2, 8.4)	0.6496 (0.4314, 0.9781) 0.0388	0.0378

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.1508
Yes	235	115 (48.9)	120 (51.1)	9.8 (7.1, 13.1)	118	56 (47.5)	62 (52.5)	4.5 (3.3, 8.1)	0.6920 (0.4995, 0.9586) 0.0268	0.0256	
No	98	44 (44.9)	54 (55.1)	13.2 (9.6, NE)	48	29 (60.4)	19 (39.6)	4.9 (2.1, 7.7)	0.4318 (0.2672, 0.6977) 0.0006	0.0005	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0112
<65	290	127 (43.8)	163 (56.2)	13.3 (11.1, 17.6)	136	68 (50.0)	68 (50.0)	4.2 (3.0, 6.0)	0.5337 (0.3940, 0.7231) 0.0001	<0.0001	
>=65	83	51 (61.4)	32 (38.6)	5.6 (4.2, 7.7)	48	24 (50.0)	24 (50.0)	7.5 (3.1, 11.4)	1.0693 (0.6549, 1.7458) 0.7888	0.7885	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1730
<75	359	170 (47.4)	189 (52.6)	11.2 (8.1, 13.6)	175	88 (50.3)	87 (49.7)	4.4 (3.1, 6.8)	0.6040 (0.4640, 0.7863) 0.0002	0.0002	
>=75	14	8 (57.1)	6 (42.9)	9.8 (3.2, NE)	9	4 (44.4)	5 (55.6)	11.1 (0.7, NE)	1.3382 (0.3995, 4.4825) 0.6366	0.6413	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Race										0.2073
White	176	83 (47.2)	93 (52.8)	11.2 (5.8, 16.1)	91	39 (42.9)	52 (57.1)	6.8 (3.2, 11.1)	0.7640 (0.5192, 1.1243) 0.1720	0.1706
Non-White	197	95 (48.2)	102 (51.8)	11.5 (7.5, 16.3)	92	53 (57.6)	39 (42.4)	4.3 (2.9, 6.1)	0.5270 (0.3727, 0.7452) 0.0003	0.0002

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.3649
Asia	147	75 (51.0)	72 (49.0)	11.8 (7.2, 21.4)	66	40 (60.6)	26 (39.4)	3.1 (1.6, 6.0)	0.5090 (0.3432, 0.7547) 0.0008	0.0007	
North America	60	25 (41.7)	35 (58.3)	11.2 (4.2, NE)	33	12 (36.4)	21 (63.6)	4.5 (1.9, NE)	0.7268 (0.3579, 1.4761) 0.3774	0.3813	
Europe + Israel	166	78 (47.0)	88 (53.0)	11.1 (7.7, 16.0)	85	40 (47.1)	45 (52.9)	7.0 (4.0, 9.0)	0.7377 (0.5008, 1.0868) 0.1238	0.1195	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.7342
0	200	103 (51.5)	97 (48.5)	9.8 (7.2, 13.1)	105	54 (51.4)	51 (48.6)	4.4 (2.1, 7.7)	0.6035 (0.4319, 0.8433) 0.0031	0.0029	
1	173	75 (43.4)	98 (56.6)	13.3 (7.4, 18.3)	79	38 (48.1)	41 (51.9)	6.0 (3.1, 8.4)	0.6779 (0.4533, 1.0137) 0.0583	0.0548	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.8511
0	60	27 (45.0)	33 (55.0)	12.5 (5.4, NE)	34	13 (38.2)	21 (61.8)	5.3 (3.0, NE)	0.7006 (0.3527, 1.3915) 0.3095	0.3156	
1	108	51 (47.2)	57 (52.8)	7.9 (4.4, NE)	51	30 (58.8)	21 (41.2)	4.4 (1.9, 7.7)	0.6635 (0.4220, 1.0432) 0.0756	0.0739	
2	115	56 (48.7)	59 (51.3)	11.1 (7.7, 13.6)	54	24 (44.4)	30 (55.6)	6.8 (3.2, NE)	0.6233 (0.3775, 1.0292) 0.0647	0.0587	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	44 (48.9)	46 (51.1)	11.4 (6.2, 18.3)	45	25 (55.6)	20 (44.4)	3.1 (1.5, 8.4)	0.5115 (0.3069, 0.8526) 0.0101	0.0087

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.9691
PD	174	78 (44.8)	96 (55.2)	11.4 (7.8, 13.9)	85	40 (47.1)	45 (52.9)	5.3 (2.1, 8.1)	0.6054 (0.4092, 0.8958) 0.0121	0.0110	
PR	48	25 (52.1)	23 (47.9)	12.4 (4.4, 22.3)	22	9 (40.9)	13 (59.1)	7.0 (0.8, NE)	0.6634 (0.3027, 1.4537) 0.3052	0.3039	
SD	82	42 (51.2)	40 (48.8)	8.5 (5.6, NE)	55	32 (58.2)	23 (41.8)	5.3 (2.9, 8.4)	0.6025 (0.3758, 0.9660) 0.0354	0.0338	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.7877
Yes	37	14 (37.8)	23 (62.2)	16.1 (5.7, NE)	15	5 (33.3)	10 (66.7)	NE (0.8, NE)	0.6465 (0.2297, 1.8195) 0.4087	0.4030	
No	336	164 (48.8)	172 (51.2)	11.1 (7.5, 13.1)	169	87 (51.5)	82 (48.5)	4.9 (3.1, 7.0)	0.6380 (0.4889, 0.8324) 0.0009	0.0008	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.4622
Yes	24	10 (41.7)	14 (58.3)	16.1 (5.4, NE)	8	2 (25.0)	6 (75.0)	NE (0.7, NE)	1.0396 (0.2240, 4.8238) 0.9605	0.9652	
No	349	168 (48.1)	181 (51.9)	11.1 (7.7, 13.2)	176	90 (51.1)	86 (48.9)	4.9 (3.1, 7.0)	0.6251 (0.4811, 0.8123) 0.0004	0.0004	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Renal function at baseline											0.0658
Normal Function	202	89 (44.1)	113 (55.9)	13.6 (7.9, 22.3)	87	43 (49.4)	44 (50.6)	4.1 (1.9, 6.0)	0.5072 (0.3478, 0.7396) 0.0004	0.0003	
Mild Impairment	123	62 (50.4)	61 (49.6)	11.1 (5.4, 16.3)	69	35 (50.7)	34 (49.3)	6.0 (2.9, 8.1)	0.6890 (0.4492, 1.0567) 0.0878	0.0840	
Moderate Impairment	41	23 (56.1)	18 (43.9)	11.1 (4.4, 11.5)	23	10 (43.5)	13 (56.5)	11.1 (5.3, NE)	1.2213 (0.5803, 2.5703) 0.5985	0.6017	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.8156
Normal Function	170	85 (50.0)	85 (50.0)	11.8 (7.8, 16.3)	98	51 (52.0)	47 (48.0)	6.0 (2.9, 8.4)	0.6276 (0.4399, 0.8953) 0.0102	0.0096	
Mild Impairment	195	91 (46.7)	104 (53.3)	11.2 (7.2, 13.3)	84	39 (46.4)	45 (53.6)	4.4 (3.1, 7.7)	0.6252 (0.4252, 0.9193) 0.0170	0.0158	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1707
Yes	332	160 (48.2)	172 (51.8)	11.1 (7.5, 13.3)	157	76 (48.4)	81 (51.6)	6.0 (3.3, 7.7)	0.6726 (0.5094, 0.8881) 0.0052	0.0049	
No	41	18 (43.9)	23 (56.1)	13.1 (6.5, NE)	27	16 (59.3)	11 (40.7)	4.4 (1.2, 5.9)	0.3860 (0.1843, 0.8083) 0.0116	0.0084	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Fatigue

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.7351
Positive	331	158 (47.7)	173 (52.3)	11.2 (8.1, 13.6)	163	81 (49.7)	82 (50.3)	5.3 (3.1, 7.5)	0.6167 (0.4692, 0.8106) 0.0005	0.0005	
Negative	42	20 (47.6)	22 (52.4)	8.4 (2.9, NE)	21	11 (52.4)	10 (47.6)	4.4 (1.5, NE)	0.7698 (0.3584, 1.6537) 0.5025	0.5003	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.2111
Positive	333	158 (47.4)	175 (52.6)	11.2 (8.5, 13.6)	166	85 (51.2)	81 (48.8)	4.5 (3.1, 7.0)	0.5931 (0.4530, 0.7764) 0.0001	0.0001	
Negative	40	20 (50.0)	20 (50.0)	8.4 (1.5, NE)	18	7 (38.9)	11 (61.1)	5.3 (3.0, NE)	1.1109 (0.4586, 2.6910) 0.8158	0.8264	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
HER2 status											
HER2 IHC 1+	214	111 (51.9)	103 (48.1)	7.5 (3.2, 10.4)	107	29 (27.1)	78 (72.9)	11.3 (8.6, NE)	1.8893 (1.2519, 2.8511) 0.0024	0.0022	0.1459
HER2 IHC 2+/ISH Negative	159	76 (47.8)	83 (52.2)	7.5 (4.2, NE)	77	29 (37.7)	48 (62.3)	9.0 (5.9, NE)	1.2351 (0.8046, 1.8958) 0.3342	0.3381	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	
Number of prior lines of chemotherapy in a metastatic setting									0.7042
1	221	105 (47.5)	116 (52.5)	8.4 (3.4, NE)	100	33 (33.0)	67 (67.0)	11.3 (8.2, NE) (0.9935, 2.1786) 0.0540	0.0555
>=2	151	81 (53.6)	70 (46.4)	6.2 (4.2, 11.1)	83	25 (30.1)	58 (69.9)	17.1 (7.5, NE) (1.0405, 2.5692) 0.0330	0.0326

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.1907
Yes	235	116 (49.4)	119 (50.6)	7.6 (4.4, 19.6)	118	39 (33.1)	79 (66.9)	9.5 (5.9, NE)	1.3367 (0.9277, 1.9261) 0.1194	0.1220	
No	98	54 (55.1)	44 (44.9)	5.7 (1.5, NE)	48	14 (29.2)	34 (70.8)	NE (8.2, NE)	2.1282 (1.1810, 3.8351) 0.0119	0.0106	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3711
<65	290	150 (51.7)	140 (48.3)	6.2 (4.3, 10.4)	136	40 (29.4)	96 (70.6)	13.3 (8.6, NE)	1.6754 (1.1800, 2.3788) 0.0039	0.0038	
>=65	83	37 (44.6)	46 (55.4)	9.3 (2.8, NE)	48	18 (37.5)	30 (62.5)	9.5 (5.9, NE)	1.2496 (0.7094, 2.2012) 0.4406	0.4479	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2048
<75	359	178 (49.6)	181 (50.4)	7.6 (5.3, 14.3)	175	55 (31.4)	120 (68.6)	9.5 (8.6, NE)	1.4920 (1.1008, 2.0222) 0.0099	0.0101	
>=75	14	9 (64.3)	5 (35.7)	2.8 (1.4, NE)	9	3 (33.3)	6 (66.7)	11.3 (6.7, NE)	4.3497 (1.1467, 16.4998) 0.0307	0.0198	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.9820
White	176	92 (52.3)	84 (47.7)	5.3 (3.0, 8.4)	91	29 (31.9)	62 (68.1)	9.0 (5.6, NE)	1.5595 (1.0249, 2.3730) 0.0380	0.0382	
Non-White	197	95 (48.2)	102 (51.8)	9.9 (5.7, NE)	92	29 (31.5)	63 (68.5)	11.3 (8.6, NE)	1.5235 (1.0033, 2.3135) 0.0482	0.0486	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.6814
Asia	147	72 (49.0)	75 (51.0)	10.2 (5.7, NE)	66	23 (34.8)	43 (65.2)	11.3 (8.6, NE)	1.3510 (0.8429, 2.1654) 0.2113	0.2158	
North America	60	31 (51.7)	29 (48.3)	4.2 (1.6, 22.3)	33	7 (21.2)	26 (78.8)	13.3 (5.9, NE)	2.1219 (0.9286, 4.8487) 0.0744	0.0686	
Europe + Israel	166	84 (50.6)	82 (49.4)	6.2 (3.0, 17.6)	85	28 (32.9)	57 (67.1)	9.0 (5.9, NE)	1.5860 (1.0318, 2.4381) 0.0355	0.0355	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.6292
0	200	100 (50.0)	100 (50.0)	8.4 (3.1, 23.0)	105	33 (31.4)	72 (68.6)	9.3 (6.7, NE)	1.4764 (0.9941, 2.1927) 0.0536	0.0543	
1	173	87 (50.3)	86 (49.7)	6.2 (4.2, 10.2)	79	25 (31.6)	54 (68.4)	11.3 (8.6, NE)	1.6486 (1.0537, 2.5793) 0.0286	0.0283	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)									0.4213
0	60	29 (48.3)	31 (51.7)	11.1 (1.4, NE)	34	9 (26.5)	25 (73.5)	9.0 (5.9, NE) 1.6774 (0.7920, 3.5527) 0.1767	0.1730
1	108	54 (50.0)	54 (50.0)	6.7 (2.8, 10.4)	51	14 (27.5)	37 (72.5)	17.1 (9.0, NE) 2.2787 (1.2646, 4.1060) 0.0061	0.0050
2	115	56 (48.7)	59 (51.3)	7.8 (4.2, NE)	54	17 (31.5)	37 (68.5)	NE (5.1, NE) 1.3906 (0.8053, 2.4015) 0.2368	0.2394

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	48 (53.3)	42 (46.7)	7.6 (3.4, 23.0)	45	18 (40.0)	27 (60.0)	8.6 (5.6, NE)	1.1898 (0.6885, 2.0562)	0.5334

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	
Best Response to last prior cancer systemic therapy									0.5954
PD	174	77 (44.3)	97 (55.7)	9.3 (4.3, NE)	85	27 (31.8)	58 (68.2)	9.5 (5.4, NE) (0.8133, 1.9612) 0.2985	0.3017
PR	48	29 (60.4)	19 (39.6)	3.4 (1.4, NE)	22	8 (36.4)	14 (63.6)	8.6 (4.2, NE) (0.7024, 3.3930) 0.2799	0.2837
SD	82	38 (46.3)	44 (53.7)	9.9 (3.2, NE)	55	15 (27.3)	40 (72.7)	17.1 (9.0, NE) (0.9673, 3.2170) 0.0641	0.0617

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.5995
Yes	37	20 (54.1)	17 (45.9)	5.7 (1.4, NE)	15	3 (20.0)	12 (80.0)	17.1 (1.4, NE)	2.2855 (0.6752, 7.7359) 0.1839	0.1744	
No	336	167 (49.7)	169 (50.3)	7.5 (4.3, 11.1)	169	55 (32.5)	114 (67.5)	9.5 (8.6, NE)	1.5128 (1.1136, 2.0550) 0.0081	0.0082	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.5492
Yes	24	9 (37.5)	15 (62.5)	NE (2.8, NE)	8	1 (12.5)	7 (87.5)	17.1 (NE, NE)	3.2147 (0.4063, 25.4323)	0.2423
No	349	178 (51.0)	171 (49.0)	6.7 (4.2, 10.2)	176	57 (32.4)	119 (67.6)	9.5 (8.2, NE)	1.5413 (1.1421, 2.0800)	0.0047

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.9905
Normal Function	202	104 (51.5)	98 (48.5)	5.8 (4.2, 19.6)	87	27 (31.0)	60 (69.0)	13.3 (6.7, NE)	1.5619 (1.0214, 2.3882) 0.0396	0.0395	
Mild Impairment	123	64 (52.0)	59 (48.0)	7.6 (2.8, 14.3)	69	22 (31.9)	47 (68.1)	9.0 (6.0, NE)	1.5067 (0.9222, 2.4616) 0.1017	0.1027	
Moderate Impairment	41	18 (43.9)	23 (56.1)	NE (3.0, NE)	23	8 (34.8)	15 (65.2)	17.1 (8.2, NE)	1.6762 (0.7259, 3.8705) 0.2264	0.2256	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hepatic function at baseline											0.8322
Normal Function	170	94 (55.3)	76 (44.7)	5.5 (1.7, 11.1)	98	35 (35.7)	63 (64.3)	9.0 (8.0, NE)	1.6114 (1.0907, 2.3808) 0.0166	0.0171	
Mild Impairment	195	91 (46.7)	104 (53.3)	7.8 (5.7, 19.6)	84	23 (27.4)	61 (72.6)	11.3 (9.3, NE)	1.4787 (0.9333, 2.3429) 0.0957	0.0951	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Baseline visceral disease										0.3014
Yes	332	165 (49.7)	167 (50.3)	7.6 (5.3, 11.1)	157	45 (28.7)	112 (71.3)	13.3 (8.6, NE)	1.6845 (1.2096, 2.3458) 0.0020	0.0019
No	41	22 (53.7)	19 (46.3)	4.2 (1.0, NE)	27	13 (48.1)	14 (51.9)	6.7 (1.5, NE)	1.1627 (0.5814, 2.3250) 0.6699	0.6809

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.8934
Positive	331	169 (51.1)	162 (48.9)	6.7 (4.3, 10.2)	163	52 (31.9)	111 (68.1)	11.3 (8.6, NE)	1.5629 (1.1438, 2.1356) 0.0051	0.0050	
Negative	42	18 (42.9)	24 (57.1)	14.3 (1.4, NE)	21	6 (28.6)	15 (71.4)	9.0 (5.9, NE)	1.4502 (0.5664, 3.7127) 0.4384	0.4433	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Nausea and Vomiting

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.7776
Positive	333	168 (50.5)	165 (49.5)	7.5 (4.3, 10.4)	166	53 (31.9)	113 (68.1)	11.3 (8.6, NE)	1.5327 (1.1239, 2.0903) 0.0070	0.0070	
Negative	40	19 (47.5)	21 (52.5)	14.3 (1.4, NE)	18	5 (27.8)	13 (72.2)	9.0 (5.9, NE)	1.6990 (0.6262, 4.6094) 0.2980	0.2984	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.2886
HER2 IHC 1+	214	81 (37.9)	133 (62.1)	16.7 (13.4, 21.7)	107	44 (41.1)	63 (58.9)	7.3 (4.4, 9.3)	0.4738 (0.3209, 0.6995)	0.0002
HER2 IHC 2+/ISH Negative	159	47 (29.6)	112 (70.4)	25.1 (15.7, NE)	77	36 (46.8)	41 (53.2)	6.1 (4.2, 14.7)	0.3628 (0.2313, 0.5689)	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.9266
1	221	81 (36.7)	140 (63.3)	16.4 (13.3, 20.0)	100	48 (48.0)	52 (52.0)	5.8 (3.0, 8.7)	0.4034 (0.2774, 0.5866) <0.0001	<0.0001	
>=2	151	46 (30.5)	105 (69.5)	23.0 (17.6, NE)	83	32 (38.6)	51 (61.4)	7.5 (4.4, 9.8)	0.4442 (0.2768, 0.7130) 0.0008	0.0006	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.2884
Yes	235	77 (32.8)	158 (67.2)	17.0 (13.9, 23.0)	118	48 (40.7)	70 (59.3)	7.3 (4.5, 9.3)	0.4315 (0.2958, 0.6294) <0.0001	<0.0001	
No	98	37 (37.8)	61 (62.2)	21.7 (13.1, NE)	48	26 (54.2)	22 (45.8)	5.4 (1.5, 9.8)	0.3591 (0.2132, 0.6047) 0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2737
<65	290	97 (33.4)	193 (66.6)	18.2 (15.7, 23.0)	136	61 (44.9)	75 (55.1)	5.9 (4.2, 8.7)	0.3924 (0.2808, 0.5486) <0.0001	<0.0001	
>=65	83	31 (37.3)	52 (62.7)	17.0 (10.2, NE)	48	19 (39.6)	29 (60.4)	7.5 (6.2, NE)	0.5825 (0.3207, 1.0581) 0.0760	0.0751	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3900
<75	359	125 (34.8)	234 (65.2)	17.6 (15.4, 23.0)	175	78 (44.6)	97 (55.4)	7.0 (4.5, 8.4)	0.4078 (0.3030, 0.5487) <0.0001	<0.0001	
>=75	14	3 (21.4)	11 (78.6)	NE (1.6, NE)	9	2 (22.2)	7 (77.8)	NE (0.7, NE)	1.1047 (0.1841, 6.6270) 0.9133	0.9133	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.3572
White	176	47 (26.7)	129 (73.3)	21.5 (16.4, NE)	91	34 (37.4)	57 (62.6)	7.7 (4.2, NE)	0.3728 (0.2350, 0.5913) <0.0001	<0.0001	
Non-White	197	81 (41.1)	116 (58.9)	17.0 (11.9, 21.7)	92	45 (48.9)	47 (51.1)	6.2 (4.4, 9.3)	0.4928 (0.3371, 0.7202) 0.0003	0.0002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.4006
Asia	147	67 (45.6)	80 (54.4)	15.7 (10.5, 21.7)	66	34 (51.5)	32 (48.5)	6.1 (2.4, 9.8)	0.4998 (0.3252, 0.7683) 0.0016	0.0013	
North America	60	11 (18.3)	49 (81.7)	21.5 (21.5, NE)	33	11 (33.3)	22 (66.7)	5.8 (2.7, NE)	0.2198 (0.0843, 0.5727) 0.0019	0.0007	
Europe + Israel	166	50 (30.1)	116 (69.9)	17.6 (15.4, NE)	85	35 (41.2)	50 (58.8)	7.5 (4.2, 16.9)	0.4325 (0.2769, 0.6754) 0.0002	0.0002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
ECOG PS											0.1138
0	200	72 (36.0)	128 (64.0)	17.0 (13.9, 25.1)	105	49 (46.7)	56 (53.3)	5.8 (2.8, 8.7)	0.3390 (0.2315, 0.4965) <0.0001	<0.0001	
1	173	56 (32.4)	117 (67.6)	21.5 (13.3, NE)	79	31 (39.2)	48 (60.8)	7.5 (5.8, NE)	0.5998 (0.3811, 0.9439) 0.0272	0.0247	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.3243
0	60	24 (40.0)	36 (60.0)	17.6 (6.9, NE)	34	15 (44.1)	19 (55.9)	5.9 (1.4, NE)	0.5254 (0.2696, 1.0237) 0.0586	0.0543
1	108	34 (31.5)	74 (68.5)	18.2 (13.1, NE)	51	18 (35.3)	33 (64.7)	9.3 (7.3, NE)	0.6230 (0.3472, 1.1179) 0.1127	0.1098
2	115	38 (33.0)	77 (67.0)	21.5 (13.3, NE)	54	21 (38.9)	33 (61.1)	7.0 (2.9, NE)	0.3844 (0.2143, 0.6894) 0.0013	0.0009

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	32 (35.6)	16.7 (13.4, NE)	45	26 (57.8)	4.2 (2.0, 7.7)	0.2704 (0.1545, 0.4731) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Pain

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.9069
PD	174	54 (31.0)	120 (69.0)	20.0 (17.0, NE)	85	35 (41.2)	50 (58.8)	7.3 (4.7, 8.7)	0.4223 (0.2704, 0.6595) 0.0002	<0.0001
PR	48	16 (33.3)	32 (66.7)	16.4 (15.7, NE)	22	7 (31.8)	15 (68.2)	NE (2.8, NE)	0.5093 (0.1981, 1.3092) 0.1613	0.1459
SD	82	30 (36.6)	52 (63.4)	21.7 (12.5, NE)	55	25 (45.5)	30 (54.5)	8.4 (4.4, 14.7)	0.4366 (0.2485, 0.7671) 0.0040	0.0031

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.0727
Yes	37	12 (32.4)	25 (67.6)	NE (8.0, NE)	15	2 (13.3)	13 (86.7)	NE (1.5, NE)	1.5158 (0.3343, 6.8725) 0.5897	0.5843	
No	336	116 (34.5)	220 (65.5)	18.2 (15.4, 23.0)	169	78 (46.2)	91 (53.8)	7.0 (4.4, 8.4)	0.3984 (0.2945, 0.5391) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0084
Yes	24	7 (29.2)	17 (70.8)	NE (5.9, NE)	8	0	8 (100)	NE (NE, NE)	NE (NE, NE) 0.9951	0.1773	
No	349	121 (34.7)	228 (65.3)	17.6 (15.4, 23.0)	176	80 (45.5)	96 (54.5)	6.2 (4.4, 8.4)	0.4025 (0.2990, 0.5417) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Renal function at baseline											0.1506
Normal Function	202	63 (31.2)	139 (68.8)	18.2 (15.4, NE)	87	39 (44.8)	48 (55.2)	7.2 (4.2, 9.3)	0.3229 (0.2107, 0.4947) <0.0001	<0.0001	
Mild Impairment	123	50 (40.7)	73 (59.3)	17.6 (10.0, NE)	69	31 (44.9)	38 (55.1)	6.1 (3.2, NE)	0.4926 (0.3071, 0.7902) 0.0033	0.0027	
Moderate Impairment	41	13 (31.7)	28 (68.3)	NE (11.2, NE)	23	7 (30.4)	16 (69.6)	NE (5.9, NE)	0.8920 (0.3542, 2.2466) 0.8085	0.8154	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.4033
Normal Function	170	68 (40.0)	102 (60.0)	16.7 (12.5, 25.1)	98	44 (44.9)	54 (55.1)	6.2 (4.5, 14.7)	0.5148 (0.3481, 0.7614) 0.0009	0.0007	
Mild Impairment	195	58 (29.7)	137 (70.3)	20.0 (13.9, NE)	84	34 (40.5)	50 (59.5)	7.7 (3.4, 9.3)	0.3708 (0.2358, 0.5830) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.4624
Yes	332	115 (34.6)	217 (65.4)	17.6 (13.9, 21.7)	157	68 (43.3)	89 (56.7)	7.2 (5.4, 8.7)	0.4460 (0.3265, 0.6092) <0.0001	<0.0001	
No	41	13 (31.7)	28 (68.3)	25.1 (16.7, NE)	27	12 (44.4)	15 (55.6)	5.9 (1.5, NE)	0.3303 (0.1388, 0.7859) 0.0123	0.0086	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.5594
Positive	331	114 (34.4)	217 (65.6)	18.2 (15.4, 23.0)	163	72 (44.2)	91 (55.8)	7.2 (4.5, 8.7)	0.4112 (0.3022, 0.5595) <0.0001	<0.0001	
Negative	42	14 (33.3)	28 (66.7)	25.1 (5.9, NE)	21	8 (38.1)	13 (61.9)	NE (1.5, NE)	0.6994 (0.2850, 1.7164) 0.4350	0.4277	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Pain

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.2337
Positive	333	113 (33.9)	220 (66.1)	18.2 (15.4, 23.0)	166	74 (44.6)	92 (55.4)	7.0 (4.5, 8.4)	0.3989 (0.2936, 0.5419) <0.0001	<0.0001	
Negative	40	15 (37.5)	25 (62.5)	17.6 (5.4, NE)	18	6 (33.3)	12 (66.7)	NE (1.5, NE)	0.9403 (0.3565, 2.4800) 0.9010	0.8945	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.3909
HER2 IHC 1+	214	70 (32.7)	144 (67.3)	24.1 (13.2, NE)	107	23 (21.5)	84 (78.5)	NE (NE, NE)	1.0077 (0.6247, 1.6258) 0.9748	0.9757
HER2 IHC 2+/ISH Negative	159	52 (32.7)	107 (67.3)	21.7 (12.6, NE)	77	24 (31.2)	53 (68.8)	9.4 (6.5, NE)	0.7134 (0.4357, 1.1680) 0.1794	0.1739

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.2868
1	221	77 (34.8)	144 (65.2)	21.7 (13.2, NE)	100	25 (25.0)	75 (75.0)	NE (NE, NE)	1.0494 (0.6649, 1.6563) 0.8358	0.8402
>=2	151	45 (29.8)	106 (70.2)	27.2 (12.6, NE)	83	22 (26.5)	61 (73.5)	13.7 (6.2, NE)	0.6331 (0.3754, 1.0676) 0.0864	0.0840

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.6026
Yes	235	74 (31.5)	161 (68.5)	21.7 (13.2, NE)	118	30 (25.4)	88 (74.6)	NE (6.5, NE)	0.7888 (0.5118, 1.2157) 0.2824	0.2805	
No	98	37 (37.8)	61 (62.2)	27.2 (12.0, NE)	48	13 (27.1)	35 (72.9)	NE (8.3, NE)	0.9840 (0.5197, 1.8632) 0.9605	0.9610	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7482
<65	290	96 (33.1)	194 (66.9)	18.0 (14.1, 27.2)	136	32 (23.5)	104 (76.5)	NE (NE, NE)	0.8659 (0.5759, 1.3020) 0.4891	0.4853	
>=65	83	26 (31.3)	57 (68.7)	NE (11.1, NE)	48	15 (31.3)	33 (68.8)	13.7 (7.5, NE)	0.8514 (0.4486, 1.6159) 0.6227	0.6220	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4669
<75	359	116 (32.3)	243 (67.7)	21.7 (15.9, NE)	175	43 (24.6)	132 (75.4)	NE (NE, NE)	0.8441 (0.5911, 1.2053) 0.3510	0.3480	
>=75	14	6 (42.9)	8 (57.1)	11.1 (0.9, NE)	9	4 (44.4)	5 (55.6)	13.7 (3.8, NE)	1.2901 (0.3624, 4.5921) 0.6942	0.6934	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Race										0.2573
White	176	49 (27.8)	127 (72.2)	NE (16.7, NE)	91	23 (25.3)	68 (74.7)	NE (6.2, NE)	0.6875 (0.4140, 1.1417) 0.1476	0.1444
Non-White	197	73 (37.1)	124 (62.9)	18.0 (11.8, 27.2)	92	24 (26.1)	68 (73.9)	NE (13.7, NE)	1.0167 (0.6374, 1.6217) 0.9446	0.9460

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.0777
Asia	147	61 (41.5)	86 (58.5)	15.9 (11.1, 27.2)	66	16 (24.2)	50 (75.8)	NE (13.7, NE)	1.2888 (0.7389, 2.2480) 0.3713	0.3706	
North America	60	13 (21.7)	47 (78.3)	NE (12.5, NE)	33	9 (27.3)	24 (72.7)	NE (3.7, NE)	0.4074 (0.1680, 0.9881) 0.0470	0.0412	
Europe + Israel	166	48 (28.9)	118 (71.1)	21.7 (16.7, NE)	85	22 (25.9)	63 (74.1)	NE (6.5, NE)	0.7304 (0.4361, 1.2234) 0.2326	0.2290	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
ECOG PS										0.3294
0	200	73 (36.5)	127 (63.5)	18.0 (13.2, 27.2)	105	23 (21.9)	82 (78.1)	NE (13.7, NE)	0.9812 (0.6085, 1.5822)	0.9359
1	173	49 (28.3)	124 (71.7)	NE (NE, NE)	79	24 (30.4)	55 (69.6)	NE (6.2, NE)	0.7536 (0.4602, 1.2340)	0.2555

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.6712
0	60	18 (30.0)	42 (70.0)	NE (11.1, NE)	34	8 (23.5)	26 (76.5)	NE (5.9, NE)	0.7320 (0.3087, 1.7359) 0.4789	0.4777	
1	108	34 (31.5)	74 (68.5)	21.7 (12.0, NE)	51	11 (21.6)	40 (78.4)	NE (NE, NE)	1.1267 (0.5646, 2.2484) 0.7351	0.7359	
2	115	42 (36.5)	73 (63.5)	16.7 (11.1, NE)	54	17 (31.5)	37 (68.5)	7.5 (5.0, NE)	0.6429 (0.3587, 1.1522) 0.1378	0.1328	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	28 (31.1)	62 (68.9)	NE (15.9, NE)	45	11 (24.4)	34 (75.6)	13.7 (6.2, NE)	0.8421 (0.4149, 1.7093) 0.6342	0.6328

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.9631
PD	174	51 (29.3)	123 (70.7)	24.1 (18.0, NE)	85	21 (24.7)	64 (75.3)	NE (7.5, NE)	0.7827 (0.4661, 1.3143) 0.3541	0.3512
PR	48	16 (33.3)	32 (66.7)	NE (10.4, NE)	22	6 (27.3)	16 (72.7)	NE (3.8, NE)	0.7773 (0.2964, 2.0388) 0.6086	0.6054
SD	82	25 (30.5)	57 (69.5)	NE (12.5, NE)	55	14 (25.5)	41 (74.5)	NE (8.3, NE)	0.8398 (0.4315, 1.6345) 0.6073	0.6043

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.7919
Yes	37	7 (18.9)	30 (81.1)	NE (NE, NE)	15	2 (13.3)	13 (86.7)	NE (1.5, NE)	0.8536 (0.1732, 4.2066)	0.8486
No	336	115 (34.2)	221 (65.8)	21.7 (13.2, NE)	169	45 (26.6)	124 (73.4)	NE (9.4, NE)	0.8745 (0.6159, 1.2417)	0.4497

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.6979
Yes	24	6 (25.0)	18 (75.0)	NE (9.6, NE)	8	1 (12.5)	7 (87.5)	NE (0.7, NE)	1.3317 (0.1575, 11.2572) 0.7925	0.7841
No	349	116 (33.2)	233 (66.8)	21.7 (14.1, NE)	176	46 (26.1)	130 (73.9)	NE (9.4, NE)	0.8478 (0.5989, 1.1999) 0.3515	0.3478

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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## Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.4641
Normal Function	202	57 (28.2)	145 (71.8)	NE (16.7, NE)	87	21 (24.1)	66 (75.9)	NE (6.7, NE)	0.7327 (0.4410, 1.2172) 0.2298	0.2255	
Mild Impairment	123	47 (38.2)	76 (61.8)	15.9 (11.8, NE)	69	16 (23.2)	53 (76.8)	NE (6.5, NE)	0.9770 (0.5421, 1.7607) 0.9382	0.9350	
Moderate Impairment	41	15 (36.6)	26 (63.4)	NE (8.5, NE)	23	7 (30.4)	16 (69.6)	NE (9.4, NE)	1.3116 (0.5342, 3.2201) 0.5539	0.5523	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.5559
Normal Function	170	65 (38.2)	105 (61.8)	18.0 (12.0, NE)	98	27 (27.6)	71 (72.4)	NE (9.4, NE)	0.9545 (0.6061, 1.5032) 0.8407	0.8399	
Mild Impairment	195	55 (28.2)	140 (71.8)	21.7 (16.7, NE)	84	19 (22.6)	65 (77.4)	NE (6.5, NE)	0.7939 (0.4659, 1.3528) 0.3960	0.3919	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.8010
Yes	332	107 (32.2)	225 (67.8)	21.7 (15.9, NE)	157	40 (25.5)	117 (74.5)	NE (13.7, NE)	0.8227 (0.5688, 1.1898) 0.2998	0.2965	
No	41	15 (36.6)	26 (63.4)	NE (5.8, NE)	27	7 (25.9)	20 (74.1)	9.4 (5.9, NE)	1.1790 (0.4733, 2.9366) 0.7236	0.7271	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Dyspnoea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (IXRS)										0.7429
Positive	331	109 (32.9)	222 (67.1)	21.7 (15.9, NE)	163	42 (25.8)	121 (74.2)	NE (13.7, NE)	0.8394 (0.5848, 1.2048) 0.3424	0.3402
Negative	42	13 (31.0)	29 (69.0)	NE (7.8, NE)	21	5 (23.8)	16 (76.2)	9.4 (5.9, NE)	1.0298 (0.3533, 3.0013) 0.9571	0.9644

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (derived)										0.9455
Positive	333	111 (33.3)	222 (66.7)	21.7 (15.9, NE)	166	43 (25.9)	123 (74.1)	NE (13.7, NE)	0.8546 (0.5977, 1.2218)	0.3862
Negative	40	11 (27.5)	29 (72.5)	NE (11.1, NE)	18	4 (22.2)	14 (77.8)	9.4 (5.9, NE)	0.8622 (0.2614, 2.8441)	0.7976

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0467
HER2 IHC 1+	214	70 (32.7)	144 (67.3)	18.6 (16.3, NE)	107	31 (29.0)	76 (71.0)	10.2 (5.8, NE)	0.7427 (0.4814, 1.1459)	0.1757	
HER2 IHC 2+/ISH Negative	159	38 (23.9)	121 (76.1)	NE (18.3, NE)	77	29 (37.7)	48 (62.3)	8.3 (5.3, NE)	0.3717 (0.2265, 0.6102)	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.1610
1	221	64 (29.0)	157 (71.0)	NE (18.3, NE)	100	30 (30.0)	70 (70.0)	10.2 (8.3, NE)	0.7155 (0.4615, 1.1092)	0.1319
>=2	151	44 (29.1)	107 (70.9)	18.6 (16.1, NE)	83	30 (36.1)	53 (63.9)	6.9 (5.3, NE)	0.3872 (0.2365, 0.6340)	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
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 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.6392
Yes	235	61 (26.0)	174 (74.0)	NE (21.7, NE)	118	33 (28.0)	85 (72.0)	10.2 (7.1, NE)	0.6287 (0.4079, 0.9688) 0.0354	0.0335	
No	98	35 (35.7)	63 (64.3)	18.6 (16.0, NE)	48	21 (43.8)	27 (56.3)	6.1 (4.7, NE)	0.4856 (0.2797, 0.8431) 0.0103	0.0090	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1873
<65	290	82 (28.3)	208 (71.7)	NE (18.3, NE)	136	46 (33.8)	90 (66.2)	10.0 (5.7, NE)	0.4993 (0.3445, 0.7236) 0.0002	0.0002	
>=65	83	26 (31.3)	57 (68.7)	18.6 (11.1, NE)	48	14 (29.2)	34 (70.8)	11.7 (8.3, NE)	0.7661 (0.3935, 1.4913) 0.4330	0.4288	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											0.1622
<75	359	102 (28.4)	257 (71.6)	NE (18.3, NE)	175	57 (32.6)	118 (67.4)	10.0 (6.1, NE)	0.5195 (0.3719, 0.7256) 0.0001	<0.0001	
>=75	14	6 (42.9)	8 (57.1)	5.8 (4.2, NE)	9	3 (33.3)	6 (66.7)	NE (0.8, NE)	1.3820 (0.3451, 5.5353) 0.6477	0.6557	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.1568
White	176	51 (29.0)	125 (71.0)	21.7 (16.0, NE)	91	34 (37.4)	57 (62.6)	5.9 (4.7, NE)	0.4248 (0.2691, 0.6704) 0.0002	0.0002	
Non-White	197	57 (28.9)	140 (71.1)	NE (16.6, NE)	92	26 (28.3)	66 (71.7)	11.7 (8.3, NE)	0.7055 (0.4405, 1.1299) 0.1466	0.1453	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Region										0.8070
Asia	147	45 (30.6)	102 (69.4)	NE (16.3, NE)	66	22 (33.3)	44 (66.7)	NE (6.1, NE)	0.6432 (0.3837, 1.0783) 0.0941	0.0918
North America	60	12 (20.0)	48 (80.0)	NE (NE, NE)	33	8 (24.2)	25 (75.8)	NE (3.1, NE)	0.5716 (0.2311, 1.4137) 0.2261	0.2184
Europe + Israel	166	51 (30.7)	115 (69.3)	18.3 (16.0, NE)	85	30 (35.3)	55 (64.7)	10.0 (5.4, 11.7)	0.4707 (0.2929, 0.7565) 0.0019	0.0015

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.4129
0	200	56 (28.0)	144 (72.0)	NE (18.6, NE)	105	34 (32.4)	71 (67.6)	10.0 (5.8, NE)	0.4802 (0.3103, 0.7430) 0.0010	0.0008	
1	173	52 (30.1)	121 (69.9)	NE (16.6, NE)	79	26 (32.9)	53 (67.1)	10.2 (6.1, NE)	0.6624 (0.4085, 1.0743) 0.0950	0.0926	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.6248
0	60	20 (33.3)	40 (66.7)	17.6 (9.7, NE)	34	13 (38.2)	21 (61.8)	5.4 (3.0, NE)	0.4081 (0.1973, 0.8443)	0.0129
1	108	28 (25.9)	80 (74.1)	21.7 (16.6, NE)	51	14 (27.5)	37 (72.5)	10.2 (7.1, NE)	0.7466 (0.3885, 1.4348)	0.3766
2	115	33 (28.7)	82 (71.3)	NE (NE, NE)	54	19 (35.2)	35 (64.8)	11.7 (4.5, NE)	0.5280 (0.2961, 0.9417)	0.0274

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	27 (30.0)	63 (70.0)	18.6 (16.1, NE)	45	14 (31.1)	31 (68.9)	9.1 (5.8, NE)	0.5070 (0.2594, 0.9910) 0.0470	0.0439

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.3244
PD	174	45 (25.9)	129 (74.1)	NE (16.3, NE)	85	25 (29.4)	60 (70.6)	NE (5.4, NE)	0.5015 (0.3024, 0.8316) 0.0075	0.0065
PR	48	12 (25.0)	36 (75.0)	NE (16.0, NE)	22	9 (40.9)	13 (59.1)	5.8 (2.8, NE)	0.2781 (0.1101, 0.7026) 0.0068	0.0038
SD	82	25 (30.5)	57 (69.5)	NE (17.6, NE)	55	17 (30.9)	38 (69.1)	10.2 (8.3, NE)	0.6886 (0.3663, 1.2945) 0.2467	0.2429

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.3094
Yes	37	11 (29.7)	26 (70.3)	NE (7.3, NE)	15	2 (13.3)	13 (86.7)	NE (2.8, NE)	1.1567 (0.2516, 5.3188) 0.8516	0.8515	
No	336	97 (28.9)	239 (71.1)	21.7 (17.6, NE)	169	58 (34.3)	111 (65.7)	10.0 (6.1, NE)	0.5316 (0.3805, 0.7426) 0.0002	0.0002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.3658
Yes	24	6 (25.0)	18 (75.0)	NE (9.6, NE)	8	1 (12.5)	7 (87.5)	NE (2.8, NE)	1.0983 (0.1274, 9.4689) 0.9320	0.9320	
No	349	102 (29.2)	247 (70.8)	NE (17.6, NE)	176	59 (33.5)	117 (66.5)	10.0 (6.1, NE)	0.5457 (0.3927, 0.7584) 0.0003	0.0003	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.3866
Normal Function	202	58 (28.7)	144 (71.3)	NE (18.3, NE)	87	27 (31.0)	60 (69.0)	NE (5.4, NE)	0.5563 (0.3486, 0.8877) 0.0139	0.0124	
Mild Impairment	123	36 (29.3)	87 (70.7)	NE (16.3, NE)	69	24 (34.8)	45 (65.2)	9.1 (5.8, NE)	0.4627 (0.2681, 0.7984) 0.0056	0.0047	
Moderate Impairment	41	12 (29.3)	29 (70.7)	NE (9.3, NE)	23	6 (26.1)	17 (73.9)	NE (5.9, NE)	1.0916 (0.4091, 2.9123) 0.8611	0.8638	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.3806
Normal Function	170	52 (30.6)	118 (69.4)	NE (18.3, NE)	98	30 (30.6)	68 (69.4)	11.7 (6.9, NE)	0.6506 (0.4116, 1.0286) 0.0659	0.0635	
Mild Impairment	195	55 (28.2)	140 (71.8)	21.7 (16.6, NE)	84	28 (33.3)	56 (66.7)	10.0 (4.9, NE)	0.4817 (0.2996, 0.7745) 0.0026	0.0021	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.0366
Yes	332	97 (29.2)	235 (70.8)	21.7 (17.6, NE)	157	46 (29.3)	111 (70.7)	11.7 (8.3, NE)	0.6404 (0.4475, 0.9165) 0.0148	0.0141	
No	41	11 (26.8)	30 (73.2)	NE (9.9, NE)	27	14 (51.9)	13 (48.1)	4.7 (2.8, NE)	0.2653 (0.1154, 0.6094) 0.0018	0.0009	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Common Symptoms/Insomnia

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.2250
Positive	331	97 (29.3)	234 (70.7)	NE (18.3, NE)	163	51 (31.3)	112 (68.7)	10.2 (7.1, NE)	0.5994 (0.4239, 0.8476) 0.0038	0.0034	
Negative	42	11 (26.2)	31 (73.8)	NE (7.8, NE)	21	9 (42.9)	12 (57.1)	5.3 (1.7, NE)	0.2679 (0.1026, 0.6992) 0.0071	0.0044	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.9490
Positive	333	95 (28.5)	238 (71.5)	NE (18.3, NE)	166	54 (32.5)	112 (67.5)	10.2 (6.9, NE)	0.5632 (0.4002, 0.7926) 0.0010	0.0008	
Negative	40	13 (32.5)	27 (67.5)	17.6 (7.4, NE)	18	6 (33.3)	12 (66.7)	5.8 (1.7, NE)	0.3974 (0.1399, 1.1290) 0.0832	0.0744	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.2752
HER2 IHC 1+	214	92 (43.0)	122 (57.0)	13.3 (9.1, 23.0)	107	31 (29.0)	76 (71.0)	11.4 (9.5, NE)	1.1576 (0.7660, 1.7493) 0.4872	0.4982	
HER2 IHC 2+/ISH Negative	159	68 (42.8)	91 (57.2)	18.2 (8.5, NE)	77	31 (40.3)	46 (59.7)	9.0 (5.1, NE)	0.8304 (0.5408, 1.2750) 0.3955	0.3890	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.3110
1	221	97 (43.9)	124 (56.1)	13.6 (8.5, 21.7)	100	32 (32.0)	68 (68.0)	11.3 (9.0, NE)	1.1640 (0.7780, 1.7415)	0.4690
>=2	151	63 (41.7)	88 (58.3)	13.3 (9.8, NE)	83	30 (36.1)	53 (63.9)	11.7 (5.9, NE)	0.8227 (0.5279, 1.2821)	0.3806

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.6603
Yes	235	100 (42.6)	135 (57.4)	13.6 (10.4, 22.3)	118	38 (32.2)	80 (67.8)	9.5 (6.2, NE)	0.9938 (0.6802, 1.4519) 0.9742	0.9628	
No	98	43 (43.9)	55 (56.1)	16.3 (8.3, NE)	48	19 (39.6)	29 (60.4)	11.3 (6.1, NE)	0.8680 (0.5030, 1.4979) 0.6112	0.6060	

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 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Age										0.8237
<65	290	123 (42.4)	167 (57.6)	18.2 (10.6, 23.0)	136	43 (31.6)	93 (68.4)	11.4 (6.2, NE)	1.0027 (0.7050, 1.4260) 0.9880	0.9993
>=65	83	37 (44.6)	46 (55.4)	11.2 (4.9, NE)	48	19 (39.6)	29 (60.4)	10.5 (6.5, 14.4)	1.0106 (0.5781, 1.7666) 0.9705	0.9759

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7462
<75	359	153 (42.6)	206 (57.4)	16.3 (10.4, 22.3)	175	56 (32.0)	119 (68.0)	11.4 (8.5, NE)	1.0275 (0.7536, 1.4009) 0.8640	0.8777	
>=75	14	7 (50.0)	7 (50.0)	8.5 (1.6, NE)	9	6 (66.7)	3 (33.3)	11.3 (0.7, NE)	0.8677 (0.2887, 2.6082) 0.8005	0.8003	

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.2551
White	176	65 (36.9)	111 (63.1)	21.7 (13.3, NE)	91	29 (31.9)	62 (68.1)	11.4 (5.1, NE)	0.8401 (0.5377, 1.3126) 0.4440	0.4387	
Non-White	197	95 (48.2)	102 (51.8)	10.4 (7.6, 18.2)	92	33 (35.9)	59 (64.1)	11.3 (8.5, NE)	1.1270 (0.7556, 1.6808) 0.5578	0.5691	

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.4153
Asia	147	77 (52.4)	70 (47.6)	10.4 (7.5, 18.2)	66	24 (36.4)	42 (63.6)	11.3 (6.1, NE)	1.2349 (0.7778, 1.9606) 0.3710	0.3784	
North America	60	16 (26.7)	44 (73.3)	22.3 (22.3, NE)	33	6 (18.2)	27 (81.8)	11.4 (11.4, NE)	1.0211 (0.3919, 2.6600) 0.9660	0.9672	
Europe + Israel	166	67 (40.4)	99 (59.6)	18.3 (9.1, NE)	85	32 (37.6)	53 (62.4)	9.0 (5.1, NE)	0.8180 (0.5333, 1.2547) 0.3573	0.3507	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.1092
0	200	80 (40.0)	120 (60.0)	21.7 (12.0, 27.2)	105	36 (34.3)	69 (65.7)	11.4 (6.5, NE)	0.7859 (0.5271, 1.1718) 0.2371	0.2321	
1	173	80 (46.2)	93 (53.8)	8.4 (5.6, NE)	79	26 (32.9)	53 (67.1)	11.3 (6.2, NE)	1.3274 (0.8491, 2.0751) 0.2141	0.2188	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.5084
0	60	25 (41.7)	35 (58.3)	NE (3.1, NE)	34	11 (32.4)	23 (67.6)	NE (2.9, NE)	1.0545 (0.5175, 2.1487)	0.8838
1	108	49 (45.4)	59 (54.6)	11.8 (7.5, 21.7)	51	17 (33.3)	34 (66.7)	10.5 (8.5, NE)	1.2217 (0.6998, 2.1328)	0.4824
2	115	41 (35.7)	74 (64.3)	22.3 (12.5, NE)	54	18 (33.3)	36 (66.7)	11.4 (5.0, NE)	0.6683 (0.3770, 1.1845)	0.1621

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	45 (50.0)	45 (50.0)	11.2 (5.1, 23.0)	45	16 (35.6)	29 (64.4)	14.4 (4.4, NE)	1.1546 (0.6484, 2.0557) 0.6254	0.6337	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.3412
PD	174	70 (40.2)	104 (59.8)	13.6 (10.2, NE)	85	30 (35.3)	55 (64.7)	9.5 (5.1, NE)	0.8105 (0.5246, 1.2523) 0.3439	0.3382	
PR	48	26 (54.2)	22 (45.8)	10.1 (1.6, NE)	22	6 (27.3)	16 (72.7)	11.7 (3.1, NE)	1.6416 (0.6701, 4.0213) 0.2782	0.2788	
SD	82	27 (32.9)	55 (67.1)	NE (13.3, NE)	55	18 (32.7)	37 (67.3)	11.4 (6.5, NE)	0.8159 (0.4461, 1.4924) 0.5090	0.5051	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.6322
Yes	37	16 (43.2)	21 (56.8)	NE (1.5, NE)	15	3 (20.0)	12 (80.0)	NE (0.8, NE)	1.5400 (0.4474, 5.3003) 0.4935	0.4907	
No	336	144 (42.9)	192 (57.1)	13.6 (10.4, 22.3)	169	59 (34.9)	110 (65.1)	11.3 (8.5, NE)	0.9580 (0.7045, 1.3026) 0.7842	0.7726	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.1250
Yes	24	12 (50.0)	12 (50.0)	5.4 (1.4, NE)	8	1 (12.5)	7 (87.5)	NE (0.8, NE)	3.8843 (0.5048, 29.8884)	0.1604
No	349	148 (42.4)	201 (57.6)	13.6 (10.4, 22.3)	176	61 (34.7)	115 (65.3)	11.3 (7.5, NE)	0.9340 (0.6902, 1.2640)	0.6450

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.5597
Normal Function	202	83 (41.1)	119 (58.9)	18.2 (10.6, 22.3)	87	28 (32.2)	59 (67.8)	NE (5.1, NE)	0.9850 (0.6388, 1.5187) 0.9454	0.9288	
Mild Impairment	123	54 (43.9)	69 (56.1)	11.8 (7.6, NE)	69	24 (34.8)	45 (65.2)	11.4 (5.8, NE)	0.9373 (0.5740, 1.5307) 0.7959	0.7932	
Moderate Impairment	41	20 (48.8)	21 (51.2)	12.5 (4.2, NE)	23	8 (34.8)	15 (65.2)	14.4 (6.5, NE)	1.5352 (0.6744, 3.4949) 0.3071	0.3055	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1566
Normal Function	170	85 (50.0)	85 (50.0)	10.6 (6.2, 18.3)	98	33 (33.7)	65 (66.3)	11.7 (9.0, NE)	1.2216 (0.8142, 1.8327) 0.3336	0.3400	
Mild Impairment	195	72 (36.9)	123 (63.1)	21.7 (11.2, NE)	84	28 (33.3)	56 (66.7)	9.5 (5.0, NE)	0.8083 (0.5183, 1.2605) 0.3478	0.3407	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1206
Yes	332	144 (43.4)	188 (56.6)	13.3 (10.4, 21.7)	157	50 (31.8)	107 (68.2)	11.4 (8.5, NE)	1.0765 (0.7775, 1.4905) 0.6570	0.6693	
No	41	16 (39.0)	25 (61.0)	NE (4.9, NE)	27	12 (44.4)	15 (55.6)	9.0 (1.2, NE)	0.6796 (0.3165, 1.4593) 0.3218	0.3164	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.8813
Positive	331	143 (43.2)	188 (56.8)	13.6 (10.4, 22.3)	163	55 (33.7)	108 (66.3)	11.3 (8.5, NE)	0.9749 (0.7115, 1.3359) 0.8745	0.8604	
Negative	42	17 (40.5)	25 (59.5)	NE (2.9, NE)	21	7 (33.3)	14 (66.7)	NE (1.0, NE)	1.2086 (0.5000, 2.9213) 0.6740	0.6662	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Appetite Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.3859
Positive	333	142 (42.6)	191 (57.4)	16.3 (10.4, 22.3)	166	57 (34.3)	109 (65.7)	11.3 (8.5, NE)	0.9454 (0.6924, 1.2909) 0.7239	0.7098	
Negative	40	18 (45.0)	22 (55.0)	8.5 (2.9, NE)	18	5 (27.8)	13 (72.2)	NE (3.4, NE)	1.5704 (0.5785, 4.2632) 0.3758	0.3706	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.4716
HER2 IHC 1+	214	86 (40.2)	128 (59.8)	15.2 (11.5, NE)	107	31 (29.0)	76 (71.0)	NE (5.9, NE)	1.0439 (0.6889, 1.5820) 0.8394	0.8412	
HER2 IHC 2+/ISH Negative	159	69 (43.4)	90 (56.6)	11.1 (7.0, NE)	77	24 (31.2)	53 (68.8)	10.1 (6.7, NE)	1.2594 (0.7898, 2.0082) 0.3326	0.3359	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.5754
1	221	95 (43.0)	126 (57.0)	12.5 (8.5, NE)	100	34 (34.0)	66 (66.0)	11.3 (5.9, NE)	1.0305 (0.6942, 1.5295)	0.8816
>=2	151	59 (39.1)	92 (60.9)	16.6 (9.7, NE)	83	21 (25.3)	62 (74.7)	NE (7.5, NE)	1.2728 (0.7696, 2.1051)	0.3474

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.8619
Yes	235	96 (40.9)	139 (59.1)	12.5 (9.7, NE)	118	33 (28.0)	85 (72.0)	NE (6.7, NE)	1.0782 (0.7223, 1.6096) 0.7126	0.7190	
No	98	42 (42.9)	56 (57.1)	16.6 (6.8, NE)	48	17 (35.4)	31 (64.6)	11.3 (6.1, NE)	1.0864 (0.6173, 1.9122) 0.7738	0.7804	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4373
<65	290	123 (42.4)	167 (57.6)	14.0 (9.9, NE)	136	37 (27.2)	99 (72.8)	NE (6.1, NE)	1.2386 (0.8547, 1.7949) 0.2584	0.2639	
>=65	83	32 (38.6)	51 (61.4)	13.4 (5.8, NE)	48	18 (37.5)	30 (62.5)	8.4 (6.7, NE)	0.9168 (0.5126, 1.6399) 0.7698	0.7709	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Age											
<75	359	147 (40.9)	212 (59.1)	14.0 (11.3, NE)	175	52 (29.7)	123 (70.3)	NE (8.3, NE)	1.0813 (0.7855, 1.4885) 0.6317	0.6408	0.1216
>=75	14	8 (57.1)	6 (42.9)	5.8 (1.4, NE)	9	3 (33.3)	6 (66.7)	11.3 (3.8, NE)	4.5256 (0.9519, 21.5169) 0.0577	0.0380	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.8310
White	176	73 (41.5)	103 (58.5)	11.5 (7.0, NE)	91	26 (28.6)	65 (71.4)	NE (5.8, NE)	1.1471 (0.7298, 1.8029) 0.5520	0.5560	
Non-White	197	82 (41.6)	115 (58.4)	14.5 (10.0, NE)	92	29 (31.5)	63 (68.5)	11.3 (8.3, NE)	1.0842 (0.7069, 1.6629) 0.7110	0.7185	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.4300
Asia	147	65 (44.2)	82 (55.8)	13.6 (9.0, NE)	66	21 (31.8)	45 (68.2)	11.3 (8.3, NE)	1.1973 (0.7296, 1.9649) 0.4761	0.4801	
North America	60	25 (41.7)	35 (58.3)	11.5 (4.3, NE)	33	6 (18.2)	27 (81.8)	NE (4.5, NE)	1.7202 (0.6938, 4.2651) 0.2417	0.2380	
Europe + Israel	166	65 (39.2)	101 (60.8)	14.5 (8.5, NE)	85	28 (32.9)	57 (67.1)	8.4 (5.9, NE)	0.9425 (0.6027, 1.4739) 0.7953	0.7915	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	200	86 (43.0)	114 (57.0)	14.0 (8.7, NE)	105	26 (24.8)	79 (75.2)	NE (8.4, NE)	1.3284 (0.8543, 2.0657) 0.2074	0.2069	0.3677
1	173	69 (39.9)	104 (60.1)	13.6 (9.0, NE)	79	29 (36.7)	50 (63.3)	9.2 (5.9, NE)	0.9461 (0.6095, 1.4686) 0.8050	0.7922	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.7353
0	60	28 (46.7)	32 (53.3)	8.1 (1.6, NE)	34	10 (29.4)	24 (70.6)	NE (4.7, NE)	1.4930 (0.7234, 3.0811) 0.2783	0.2775	
1	108	42 (38.9)	66 (61.1)	11.5 (7.1, NE)	51	17 (33.3)	34 (66.7)	NE (5.8, NE)	1.1092 (0.6308, 1.9505) 0.7190	0.7218	
2	115	52 (45.2)	63 (54.8)	13.6 (8.7, NE)	54	14 (25.9)	40 (74.1)	NE (6.7, NE)	1.1861 (0.6493, 2.1667) 0.5788	0.5793	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	33 (36.7)	57 (63.3)	NE (9.9, NE)	45	14 (31.1)	31 (68.9)	9.2 (5.9, NE)	0.8934 (0.4734, 1.6861) 0.7279	0.7179

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.7318
PD	174	65 (37.4)	109 (62.6)	14.5 (9.9, NE)	85	22 (25.9)	63 (74.1)	NE (7.5, NE)	1.1213 (0.6888, 1.8254) 0.6452	0.6473
PR	48	18 (37.5)	30 (62.5)	22.3 (8.1, NE)	22	7 (31.8)	15 (68.2)	6.7 (4.7, NE)	0.7488 (0.3070, 1.8261) 0.5248	0.5170
SD	82	36 (43.9)	46 (56.1)	12.5 (7.0, NE)	55	18 (32.7)	37 (67.3)	11.3 (6.1, NE)	1.1293 (0.6379, 1.9994) 0.6764	0.6811

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.0899
Yes	37	14 (37.8)	23 (62.2)	NE (4.2, NE)	15	1 (6.7)	14 (93.3)	NE (5.9, NE)	4.5902 (0.6013, 35.0404) 0.1417	0.1064
No	336	141 (42.0)	195 (58.0)	13.6 (10.0, NE)	169	54 (32.0)	115 (68.0)	11.3 (7.5, NE)	1.0651 (0.7760, 1.4619) 0.6964	0.7068

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.3851
Yes	24	8 (33.3)	16 (66.7)	NE (4.2, NE)	8	1 (12.5)	7 (87.5)	NE (5.9, NE)	2.5821 (0.3206, 20.7964) 0.3728	0.3551	
No	349	147 (42.1)	202 (57.9)	13.6 (10.0, NE)	176	54 (30.7)	122 (69.3)	11.3 (8.3, NE)	1.1071 (0.8081, 1.5167) 0.5265	0.5350	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Renal function at baseline										0.2890
Normal Function	202	90 (44.6)	112 (55.4)	13.4 (8.1, NE)	87	26 (29.9)	61 (70.1)	10.1 (5.9, NE)	1.1417 (0.7345, 1.7746) 0.5558	0.5640
Mild Impairment	123	48 (39.0)	75 (61.0)	NE (8.1, NE)	69	23 (33.3)	46 (66.7)	8.3 (5.8, NE)	0.9255 (0.5591, 1.5321) 0.7633	0.7565
Moderate Impairment	41	17 (41.5)	24 (58.5)	15.2 (5.8, NE)	23	5 (21.7)	18 (78.3)	NE (11.3, NE)	2.1957 (0.8081, 5.9660) 0.1230	0.1140

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.9840
Normal Function	170	77 (45.3)	93 (54.7)	13.4 (8.1, NE)	98	32 (32.7)	66 (67.3)	NE (7.5, NE)	1.1208 (0.7393, 1.6992) 0.5912	0.5956	
Mild Impairment	195	77 (39.5)	118 (60.5)	14.0 (9.8, NE)	84	23 (27.4)	61 (72.6)	11.3 (5.8, NE)	1.1568 (0.7230, 1.8510) 0.5435	0.5471	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1852
Yes	332	138 (41.6)	194 (58.4)	13.4 (9.9, NE)	157	43 (27.4)	114 (72.6)	NE (9.2, NE)	1.2390 (0.8777, 1.7491) 0.2232	0.2252	
No	41	17 (41.5)	24 (58.5)	14.5 (5.1, NE)	27	12 (44.4)	15 (55.6)	5.9 (4.4, NE)	0.7170 (0.3364, 1.5279) 0.3887	0.3810	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.8034
Positive	331	138 (41.7)	193 (58.3)	14.0 (10.1, NE)	163	47 (28.8)	116 (71.2)	NE (8.4, NE)	1.1444 (0.8197, 1.5977) 0.4282	0.4332	
Negative	42	17 (40.5)	25 (59.5)	12.3 (1.6, NE)	21	8 (38.1)	13 (61.9)	5.9 (4.4, NE)	1.0972 (0.4687, 2.5681) 0.8308	0.8384	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Constipation

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.4282
Positive	333	136 (40.8)	197 (59.2)	14.0 (11.1, NE)	166	50 (30.1)	116 (69.9)	11.3 (8.3, NE)	1.0768 (0.7765, 1.4932)	0.6652	
Negative	40	19 (47.5)	21 (52.5)	9.8 (1.5, NE)	18	5 (27.8)	13 (72.2)	NE (5.8, NE)	1.6683 (0.6168, 4.5127)	0.3073	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
HER2 status											
HER2 IHC 1+	214	55 (25.7)	159 (74.3)	NE (NE, NE)	107	19 (17.8)	88 (82.2)	NE (11.4, NE)	1.0443 (0.6147, 1.7741)	0.8772	0.9034
HER2 IHC 2+/ISH Negative	159	46 (28.9)	113 (71.1)	NE (16.8, NE)	77	17 (22.1)	60 (77.9)	14.4 (9.0, NE)	1.0162 (0.5789, 1.7839)	0.9651	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.2200
1	221	66 (29.9)	155 (70.1)	NE (18.0, NE)	100	18 (18.0)	82 (82.0)	NE (11.4, NE)	1.2297 (0.7252, 2.0851) 0.4429	0.4446
>=2	151	35 (23.2)	116 (76.8)	NE (NE, NE)	83	18 (21.7)	65 (78.3)	14.4 (9.0, NE)	0.8305 (0.4669, 1.4774) 0.5274	0.5167

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.5219
Yes	235	68 (28.9)	167 (71.1)	NE (18.0, NE)	118	22 (18.6)	96 (81.4)	NE (9.2, NE)	1.1091 (0.6807, 1.8072) 0.6776	0.6786	
No	98	21 (21.4)	77 (78.6)	NE (NE, NE)	48	9 (18.8)	39 (81.3)	NE (11.4, NE)	0.8239 (0.3720, 1.8249) 0.6331	0.6242	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9446
<65	290	80 (27.6)	210 (72.4)	NE (21.7, NE)	136	26 (19.1)	110 (80.9)	NE (9.3, NE)	1.0139 (0.6468, 1.5892) 0.9522	0.9627	
>=65	83	21 (25.3)	62 (74.7)	NE (NE, NE)	48	10 (20.8)	38 (79.2)	14.4 (11.4, NE)	1.0352 (0.4814, 2.2261) 0.9294	0.9279	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Age											
<75	359	94 (26.2)	265 (73.8)	NE (21.7, NE)	175	33 (18.9)	142 (81.1)	NE (11.4, NE)	1.0095 (0.6747, 1.5104) 0.9633	0.9733	0.3930
>=75	14	7 (50.0)	7 (50.0)	14.1 (1.6, NE)	9	3 (33.3)	6 (66.7)	14.4 (0.8, NE)	1.7818 (0.4531, 7.0072) 0.4084	0.4021	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.2200
White	176	57 (32.4)	119 (67.6)	21.7 (14.1, NE)	91	17 (18.7)	74 (81.3)	NE (9.2, NE)	1.3375 (0.7716, 2.3182) 0.3001	0.3012	
Non-White	197	44 (22.3)	153 (77.7)	NE (NE, NE)	92	19 (20.7)	73 (79.3)	14.4 (9.5, NE)	0.7827 (0.4536, 1.3504) 0.3786	0.3723	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.2715
Asia	147	32 (21.8)	115 (78.2)	NE (NE, NE)	66	15 (22.7)	51 (77.3)	14.4 (9.3, NE)	0.6945 (0.3734, 1.2918) 0.2496	0.2436	
North America	60	17 (28.3)	43 (71.7)	NE (9.1, NE)	33	6 (18.2)	27 (81.8)	13.3 (NE, NE)	0.9692 (0.3710, 2.5320) 0.9490	0.9528	
Europe + Israel	166	52 (31.3)	114 (68.7)	21.7 (16.8, NE)	85	15 (17.6)	70 (82.4)	NE (9.5, NE)	1.4408 (0.8043, 2.5811) 0.2195	0.2201	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	200	58 (29.0)	142 (71.0)	NE (18.0, NE)	105	22 (21.0)	83 (79.0)	NE (9.5, NE)	0.9390 (0.5702, 1.5463) 0.8047	0.8005	0.6017
1	173	43 (24.9)	130 (75.1)	NE (NE, NE)	79	14 (17.7)	65 (82.3)	NE (9.2, NE)	1.1760 (0.6389, 2.1646) 0.6026	0.6104	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1439
0	60	18 (30.0)	42 (70.0)	16.8 (12.5, NE)	34	6 (17.6)	28 (82.4)	NE (9.0, NE)	1.2112 (0.4747, 3.0905) 0.6885	0.6908	
1	108	29 (26.9)	79 (73.1)	NE (21.7, NE)	51	10 (19.6)	41 (80.4)	NE (9.5, NE)	1.1745 (0.5683, 2.4273) 0.6641	0.6681	
2	115	32 (27.8)	83 (72.2)	NE (14.3, NE)	54	6 (11.1)	48 (88.9)	NE (NE, NE)	1.7953 (0.7403, 4.3540) 0.1954	0.1907	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	22 (24.4)	68 (75.6)	NE (18.0, NE)	45	14 (31.1)	31 (68.9)	9.3 (8.6, NE)	0.5279 (0.2655, 1.0496) 0.0685	0.0641

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.4907
PD	174	53 (30.5)	121 (69.5)	NE (13.5, NE)	85	13 (15.3)	72 (84.7)	NE (9.5, NE)	1.5436 (0.8348, 2.8543) 0.1663	0.1658	
PR	48	11 (22.9)	37 (77.1)	NE (NE, NE)	22	4 (18.2)	18 (81.8)	NE (8.6, NE)	0.7722 (0.2405, 2.4791) 0.6640	0.6558	
SD	82	24 (29.3)	58 (70.7)	NE (16.8, NE)	55	12 (21.8)	43 (78.2)	NE (9.0, NE)	1.1400 (0.5662, 2.2953) 0.7137	0.7111	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.0107
Yes	37	13 (35.1)	24 (64.9)	16.1 (5.9, NE)	15	0	15 (100)	NE (NE, NE)	NE (NE, NE) 0.9935	0.0721	
No	336	88 (26.2)	248 (73.8)	NE (21.7, NE)	169	36 (21.3)	133 (78.7)	14.4 (11.4, NE)	0.9249 (0.6237, 1.3715) 0.6977	0.6871	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0794
Yes	24	7 (29.2)	17 (70.8)	NE (5.9, NE)	8	0	8 (100)	NE (NE, NE)	NE (NE, NE) 0.9956	0.2366	
No	349	94 (26.9)	255 (73.1)	NE (21.7, NE)	176	36 (20.5)	140 (79.5)	14.4 (11.4, NE)	0.9882 (0.6690, 1.4598) 0.9526	0.9415	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Renal function at baseline										0.3489
Normal Function	202	56 (27.7)	146 (72.3)	NE (16.8, NE)	87	12 (13.8)	75 (86.2)	NE (13.3, NE)	1.4015 (0.7453, 2.6351) 0.2948	0.2972
Mild Impairment	123	35 (28.5)	88 (71.5)	NE (18.0, NE)	69	16 (23.2)	53 (76.8)	NE (9.0, NE)	0.8951 (0.4879, 1.6423) 0.7205	0.7197
Moderate Impairment	41	9 (22.0)	32 (78.0)	NE (13.5, NE)	23	7 (30.4)	16 (69.6)	14.4 (9.5, NE)	0.7409 (0.2749, 1.9970) 0.5534	0.5523

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Diarrhea

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.7064
Normal Function	170	54 (31.8)	116 (68.2)	NE (16.8, NE)	98	21 (21.4)	77 (78.6)	NE (11.4, NE)	1.0943 (0.6563, 1.8244) 0.7298	0.7339
Mild Impairment	195	46 (23.6)	149 (76.4)	NE (21.7, NE)	84	15 (17.9)	69 (82.1)	13.3 (9.3, NE)	0.9515 (0.5258, 1.7216) 0.8694	0.8659

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1681
Yes	332	90 (27.1)	242 (72.9)	NE (21.7, NE)	157	27 (17.2)	130 (82.8)	NE (11.4, NE)	1.1611 (0.7512, 1.7946) 0.5014	0.5041	
No	41	11 (26.8)	30 (73.2)	NE (16.8, NE)	27	9 (33.3)	18 (66.7)	9.0 (5.3, NE)	0.6516 (0.2618, 1.6215) 0.3571	0.3448	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (IXRS)										0.9649
Positive	331	89 (26.9)	242 (73.1)	NE (21.7, NE)	163	31 (19.0)	132 (81.0)	NE (11.4, NE)	1.0315 (0.6816, 1.5611)	0.8873
Negative	42	12 (28.6)	30 (71.4)	NE (7.8, NE)	21	5 (23.8)	16 (76.2)	9.0 (5.3, NE)	0.9989 (0.3424, 2.9139)	0.9886

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (derived)										0.7022
Positive	333	89 (26.7)	244 (73.3)	NE (21.7, NE)	166	31 (18.7)	135 (81.3)	NE (11.4, NE)	1.0564 (0.6980, 1.5989) 0.7952	0.8006
Negative	40	12 (30.0)	28 (70.0)	NE (7.8, NE)	18	5 (27.8)	13 (72.2)	9.0 (5.3, NE)	0.8226 (0.2813, 2.4051) 0.7212	0.7127

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.9682
HER2 IHC 1+	214	47 (22.0)	167 (78.0)	NE (NE, NE)	107	25 (23.4)	82 (76.6)	18.5 (11.3, NE)	0.5899 (0.3575, 0.9733) 0.0389	0.0366
HER2 IHC 2+/ISH Negative	159	32 (20.1)	127 (79.9)	28.1 (20.9, NE)	77	17 (22.1)	60 (77.9)	17.5 (17.5, NE)	0.5925 (0.3247, 1.0812) 0.0881	0.0848

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Number of prior lines of chemotherapy in a metastatic setting									0.6533	
1	221	46 (20.8)	175 (79.2)	NE (NE, NE)	100	23 (23.0)	77 (77.0)	17.5 (11.3, NE)	0.6693 (0.4024, 1.1133)	0.1192
>=2	151	32 (21.2)	119 (78.8)	28.1 (NE, NE)	83	19 (22.9)	64 (77.1)	18.5 (6.9, NE)	0.4751 (0.2621, 0.8615)	0.0123

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Prior CDK4/6										0.6891
Yes	235	50 (21.3)	185 (78.7)	NE (20.9, NE)	118	24 (20.3)	94 (79.7)	18.5 (18.5, NE)	0.6861 (0.4173, 1.1279) 0.1375	0.1359
No	98	21 (21.4)	77 (78.6)	NE (NE, NE)	48	12 (25.0)	36 (75.0)	17.5 (8.6, NE)	0.5402 (0.2605, 1.1203) 0.0980	0.0923

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3228
<65	290	61 (21.0)	229 (79.0)	NE (NE, NE)	136	33 (24.3)	103 (75.7)	17.5 (17.5, NE)	0.5464 (0.3543, 0.8428) 0.0063	0.0055	
>=65	83	18 (21.7)	65 (78.3)	28.1 (17.8, NE)	48	9 (18.8)	39 (81.3)	18.5 (8.6, NE)	0.6914 (0.2980, 1.6040) 0.3900	0.3868	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Age											
<75	359	74 (20.6)	285 (79.4)	28.1 (28.1, NE)	175	39 (22.3)	136 (77.7)	18.5 (17.5, NE)	0.5730 (0.3845, 0.8541) 0.0063	0.0056	0.3558
>=75	14	5 (35.7)	9 (64.3)	17.8 (1.6, NE)	9	3 (33.3)	6 (66.7)	11.3 (3.5, NE)	0.9579 (0.2118, 4.3324) 0.9555	0.9556	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Race										0.8889
White	176	38 (21.6)	138 (78.4)	NE (20.9, NE)	91	20 (22.0)	71 (78.0)	18.5 (NE, NE)	0.6635 (0.3801, 1.1581) 0.1489	0.1453
Non-White	197	41 (20.8)	156 (79.2)	28.1 (28.1, NE)	92	22 (23.9)	70 (76.1)	17.5 (11.3, NE)	0.5241 (0.3073, 0.8938) 0.0177	0.0160

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.9031
Asia	147	33 (22.4)	114 (77.6)	28.1 (28.1, NE)	66	18 (27.3)	48 (72.7)	17.5 (11.3, NE)	0.4764 (0.2633, 0.8620) 0.0142	0.0123	
North America	60	10 (16.7)	50 (83.3)	NE (20.9, NE)	33	5 (15.2)	28 (84.8)	NE (4.4, NE)	0.7879 (0.2616, 2.3732) 0.6718	0.6720	
Europe + Israel	166	36 (21.7)	130 (78.3)	NE (NE, NE)	85	19 (22.4)	66 (77.6)	18.5 (NE, NE)	0.6723 (0.3803, 1.1885) 0.1719	0.1681	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS									
0	200	45 (22.5)	155 (77.5) (20.9, NE)	105	21 (20.0)	84 (80.0) (17.5, NE)	0.6918 (0.4073, 1.1750) 0.1728	0.1707	0.4035
1	173	34 (19.7)	139 (80.3) (NE, NE)	79	21 (26.6)	58 (73.4) (7.0, NE)	0.4679 (0.2648, 0.8268) 0.0089	0.0075	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.1952
0	60	12 (20.0)	48 (80.0)	NE (17.8, NE)	34	9 (26.5)	25 (73.5)	17.5 (5.9, NE)	0.3505 (0.1396, 0.8798)	0.0204
1	108	21 (19.4)	87 (80.6)	NE (15.9, NE)	51	11 (21.6)	40 (78.4)	18.5 (11.3, NE)	0.6693 (0.3179, 1.4089)	0.2872
2	115	22 (19.1)	93 (80.9)	NE (NE, NE)	54	15 (27.8)	39 (72.2)	NE (6.7, NE)	0.4031 (0.2028, 0.8014)	0.0074

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	24 (26.7)	66 (73.3)	28.1 (28.1, NE)	45	7 (15.6)	38 (84.4)	NE (NE, NE)	1.1454 (0.4839, 2.7112) 0.7574	0.7591

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Best Response to last prior cancer systemic therapy									0.9928	
PD	174	35 (20.1)	139 (79.9)	28.1 (NE, NE)	85	20 (23.5)	65 (76.5)	18.5 (8.6, NE)	0.5878 (0.3341, 1.0342) 0.0653	0.0616
PR	48	12 (25.0)	36 (75.0)	NE (17.8, NE)	22	5 (22.7)	17 (77.3)	NE (6.7, NE)	0.5727 (0.1936, 1.6945) 0.3139	0.3121
SD	82	19 (23.2)	63 (76.8)	NE (15.9, NE)	55	14 (25.5)	41 (74.5)	17.5 (11.3, NE)	0.5344 (0.2621, 1.0898) 0.0848	0.0809

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Reported history of CNS metastases										0.2046
Yes	37	8 (21.6)	29 (78.4)	20.9 (20.9, NE)	15	1 (6.7)	14 (93.3)	NE (NE, NE)	2.0858 (0.2529, 17.1989)	0.4850
No	336	71 (21.1)	265 (78.9)	28.1 (28.1, NE)	169	41 (24.3)	128 (75.7)	17.5 (11.3, NE)	0.5471 (0.3681, 0.8131)	0.0025

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0894
Yes	24	4 (16.7)	20 (83.3)	16.5 (16.5, NE)	8	0	8 (100)	NE (NE, NE)	NE (NE, NE) 0.9962	0.2697	
No	349	75 (21.5)	274 (78.5)	28.1 (28.1, NE)	176	42 (23.9)	134 (76.1)	17.5 (11.3, NE)	0.5656 (0.3833, 0.8348) 0.0041	0.0037	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Renal function at baseline										0.2219
Normal Function	202	47 (23.3)	155 (76.7)	NE (20.9, NE)	87	21 (24.1)	66 (75.9)	17.5 (8.6, NE)	0.6450 (0.3821, 1.0886) 0.1006	0.0974
Mild Impairment	123	21 (17.1)	102 (82.9)	28.1 (NE, NE)	69	16 (23.2)	53 (76.8)	NE (8.4, NE)	0.3473 (0.1700, 0.7094) 0.0037	0.0026
Moderate Impairment	41	10 (24.4)	31 (75.6)	NE (11.2, NE)	23	5 (21.7)	18 (78.3)	18.5 (11.3, NE)	0.9970 (0.3375, 2.9452) 0.9957	0.9957

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.3668
Normal Function	170	39 (22.9)	131 (77.1)	28.1 (20.9, NE)	98	27 (27.6)	71 (72.4)	17.5 (8.6, NE)	0.5258 (0.3169, 0.8724) 0.0128	0.0115
Mild Impairment	195	40 (20.5)	155 (79.5)	NE (NE, NE)	84	15 (17.9)	69 (82.1)	18.5 (11.3, NE)	0.6947 (0.3776, 1.2780) 0.2415	0.2381

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:29; Program name: T3\_EQ5D\_FD\_2\_FAS.sas; Output name: T25C30.rtf

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DE.T.7.2.2 - EORTC QLQ-C30 - Definitive deterioration 10 points - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - Full Analysis Set

Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline visceral disease										0.1147
Yes	332	69 (20.8)	263 (79.2)	NE (NE, NE)	157	32 (20.4)	125 (79.6)	17.5 (17.5, NE)	0.6818 (0.4444, 1.0461) 0.0795	0.0775
No	41	10 (24.4)	31 (75.6)	28.1 (13.1, NE)	27	10 (37.0)	17 (63.0)	6.7 (4.4, NE)	0.2700 (0.1031, 0.7067) 0.0076	0.0047

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 10JAN2023 – 19:29; Program name: T3\_EQ5D\_FD\_2\_FAS.sas; Output name: T25C30.rtf

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Common Symptoms/Financial Difficulties

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)										0.4134	
Positive	331	69 (20.8)	262 (79.2)	NE (NE, NE)	163	35 (21.5)	128 (78.5)	17.5 (17.5, NE)	0.6263 (0.4130, 0.9497)	0.0263	
Negative	42	10 (23.8)	32 (76.2)	28.1 (8.8, NE)	21	7 (33.3)	14 (66.7)	7.0 (4.4, NE)	0.3736 (0.1305, 1.0694)	0.0561	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:29; Program name: T3\_EQ5D\_FD\_2\_FAS.sas; Output name: T25C30.rtf

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Common Symptoms/Financial Difficulties

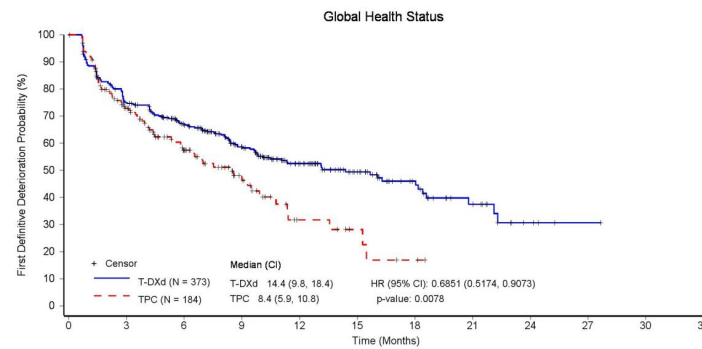
Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (derived)										0.3390
Positive	333	70 (21.0)	263 (79.0)	NE (NE, NE)	166	36 (21.7)	130 (78.3)	17.5 (11.3, NE)	0.6291 (0.4167, 0.9496)	0.0260
Negative	40	9 (22.5)	31 (77.5)	28.1 (17.8, NE)	18	6 (33.3)	12 (66.7)	7.0 (1.7, NE)	0.3092 (0.1002, 0.9542)	0.0318

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:29; Program name: T3\_EQ5D\_FD\_2\_FAS.sas; Output name: T25C30.rtf

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Patients still at risk:

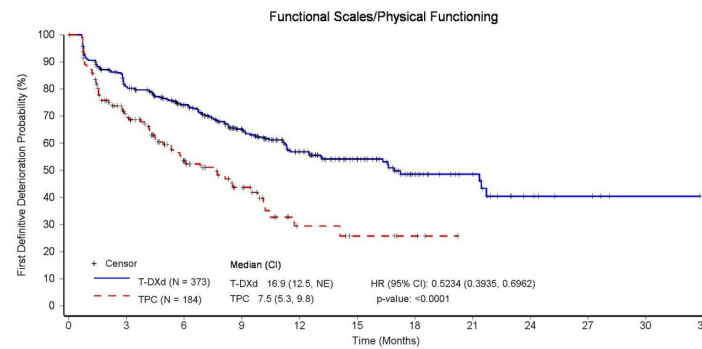
T-DXd (N = 373)	373	251	195	139	83	54	31	16	4	1	0	0
TPC (N = 184)	184	99	54	27	9	5	2	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:30; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F26C30.rtf

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Patients still at risk:

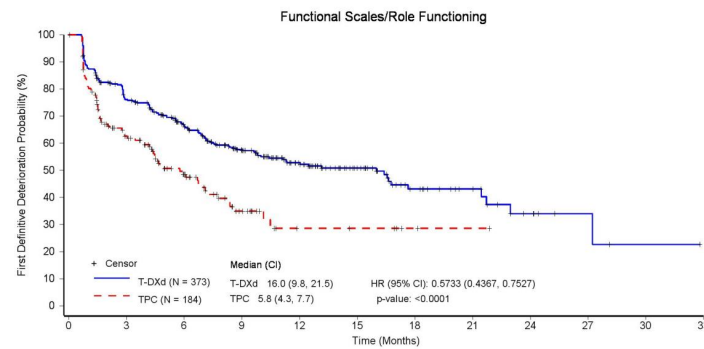
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	270	212	155	96	62	33	20	7	4	1	0
TPC (N = 184)	184	96	50	26	8	5	3	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

T-DXd (N = 373)	373	251	193	137	85	51	28	17	7	3	1	0
TPC (N = 184)	184	83	45	19	6	5	2	1	0	0	0	0

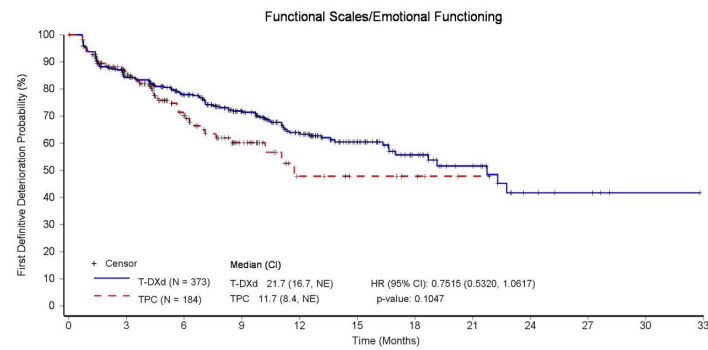
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

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Patients still at risk:

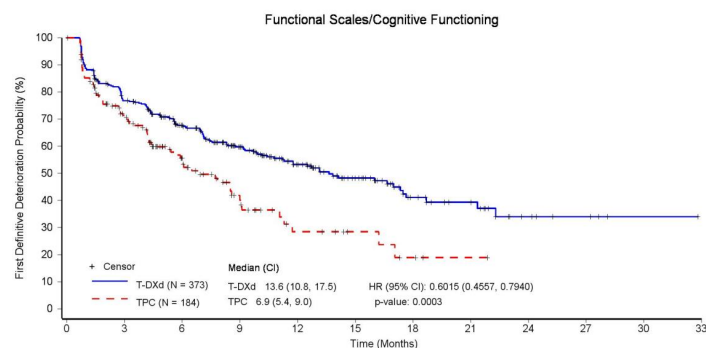
T-DXd (N = 373)	373	280	226	168	109	67	38	20	6	4	1	0
TPC (N = 184)	184	114	60	27	9	6	4	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:30; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F26C30.rtf

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Patients still at risk:

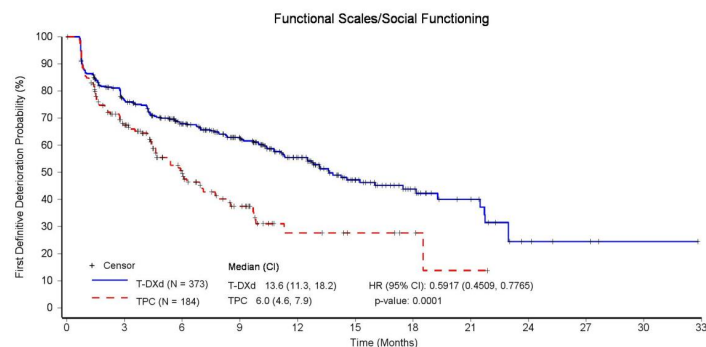
T-DXd (N = 373)	373	252	191	138	90	55	29	18	7	4	1	0
TPC (N = 184)	184	99	50	24	10	6	3	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

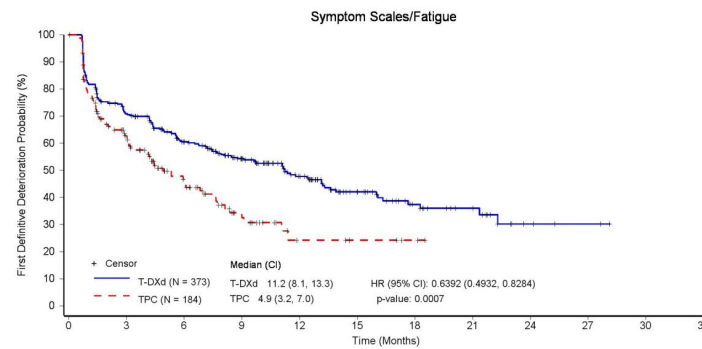
T-DXd (N = 373)	373	251	191	146	92	50	29	16	5	3	1	0
TPC (N = 184)	184	97	50	25	8	5	3	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

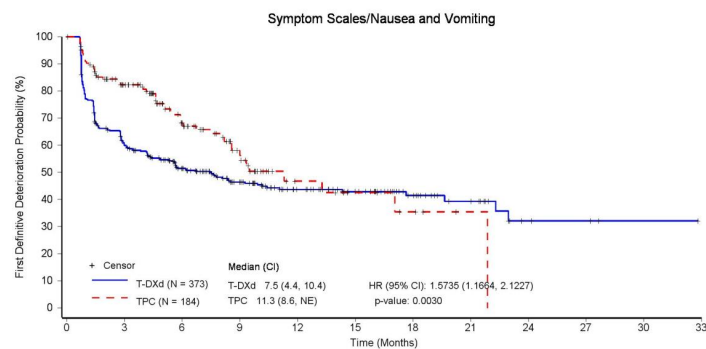
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	235	176	133	82	45	26	16	4	2	0	0
TPC (N = 184)	184	85	44	19	6	4	2	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

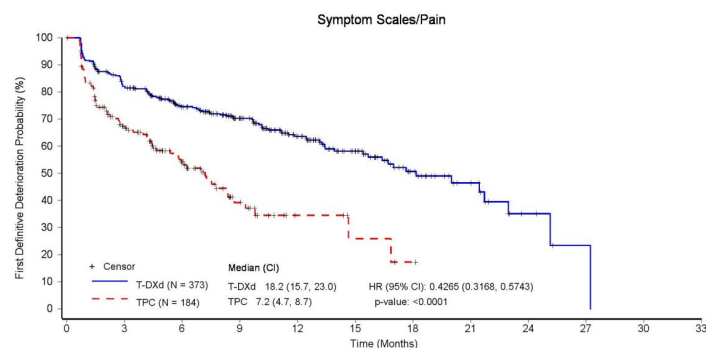
T-DXd (N = 373)	373	198	141	97	65	48	28	17	4	3	1	0
TPC (N = 184)	184	111	62	32	11	7	4	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:30; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F26C30.rtf

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Patients still at risk:

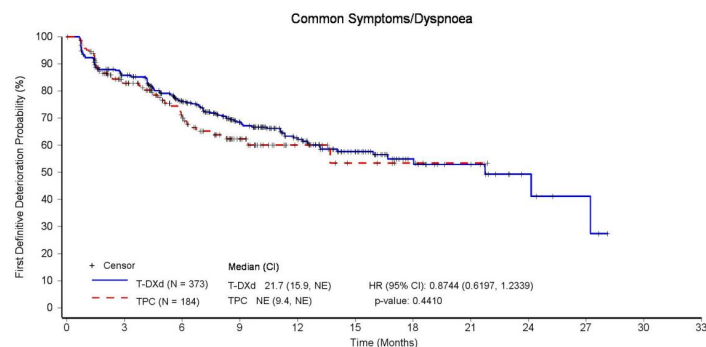
T-DXd (N = 373)	373	271	208	159	99	59	32	16	4	1	0	0
TPC (N = 184)	184	91	49	20	6	3	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

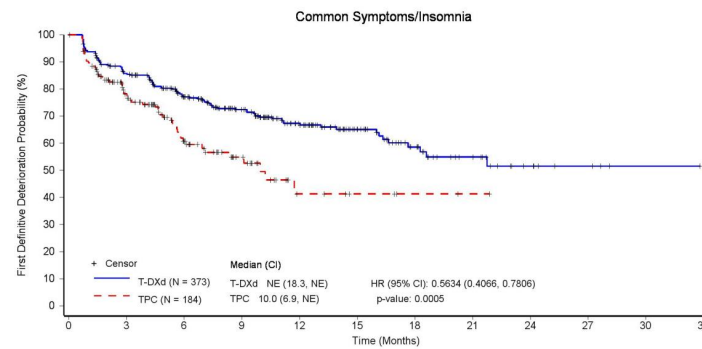
T-DXd (N = 373)	373	282	214	152	101	59	27	18	6	3	0	0
TPC (N = 184)	184	108	63	32	11	6	3	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	282	213	161	106	64	36	20	8	4	1	0
TPC (N = 184)	184	103	52	26	7	4	2	1	0	0	0	0

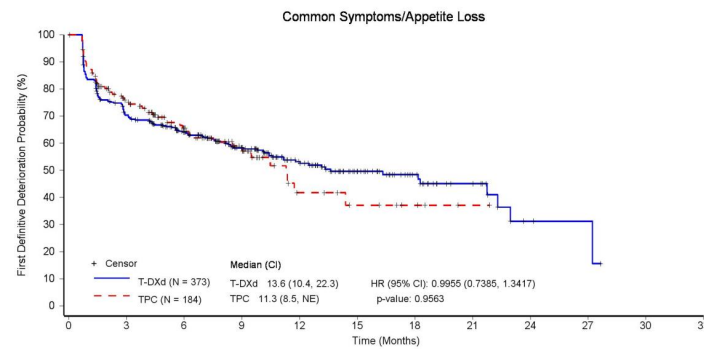
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:30; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F26C30.rtf



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Patients still at risk:

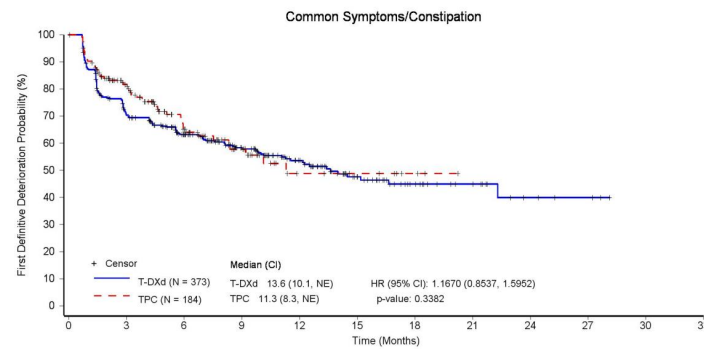
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T-DXd (N = 373)	373	237	183	137	86	50	30	15	3	2	0	0
TPC (N = 184)	184	103	59	32	11	7	4	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:30; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F26C30.rtf

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Patients still at risk:

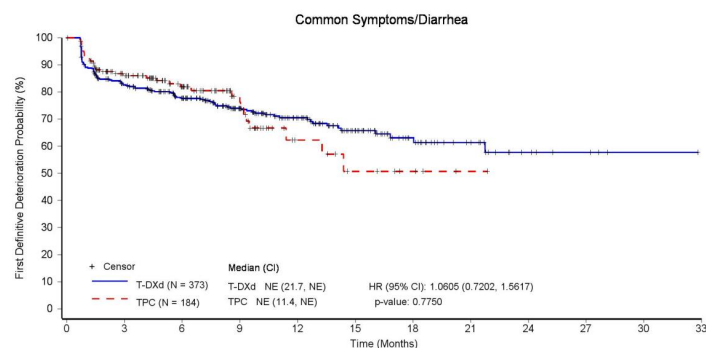
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	232	175	129	78	42	24	14	5	3	0	0
TPC (N = 184)	184	107	58	28	11	7	3	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:30; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F26C30.rtf

Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.7.2.3 - EORTC QLQ-C30 - Definitive deterioration 10 points - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - Full Analysis Set

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Patients still at risk:

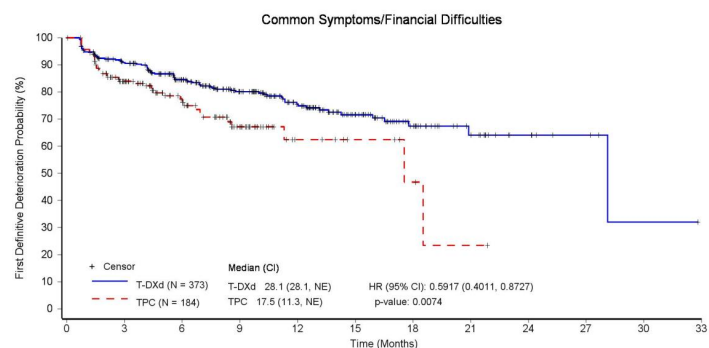
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	269	219	162	109	65	36	21	7	4	1	0
TPC (N = 184)	184	112	66	35	12	7	4	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:30; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F26C30.rtf

Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.7.2.3 - EORTC QLQ-C30 - Definitive deterioration 10 points - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - Full Analysis Set

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Patients still at risk:

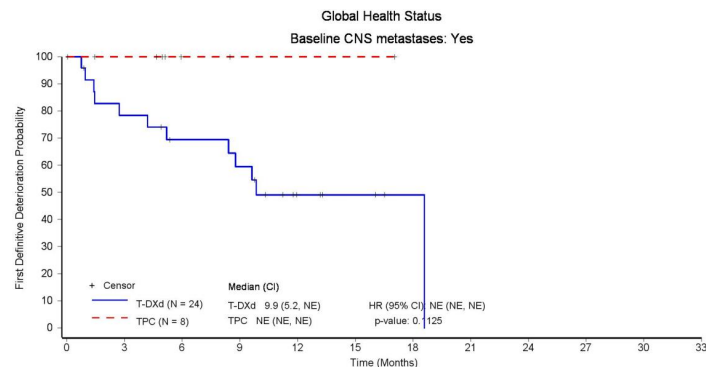
T-DXd (N = 373)	373	292	230	173	115	70	39	19	8	4	1	0
TPC (N = 184)	184	112	64	32	10	6	3	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:30; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F26C30.rtf

Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 24)	24	18	14	12	5	3	1	0	0	0	0	0
TPC (N = 8)	8	6	2	1	1	1	0	0	0	0	0	0

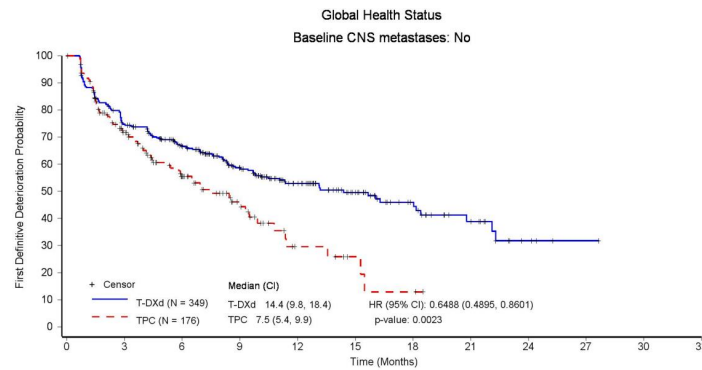
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:31; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F27C30.rtf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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DE.F.7.2.4 - EORTC QLQ-C30 - Definitive deterioration 10 points - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO  
 11-Jan-2022 - Full Analysis Set



Patients still at risk:	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 349)	349	233	181	127	78	51	30	16	4	1	0	0
TPC (N = 176)	176	93	52	26	8	4	2	0	0	0	0	0

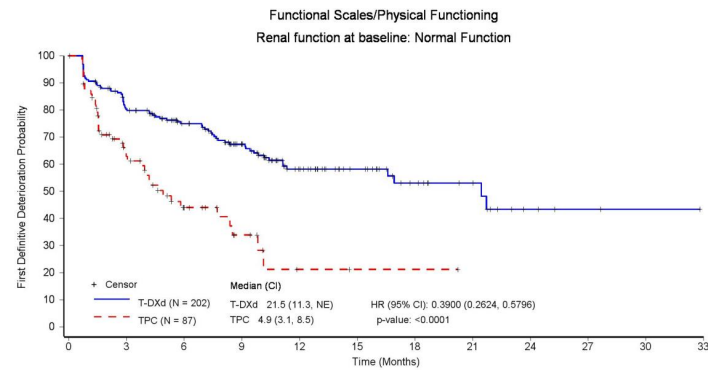
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:31; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F27C30.rtf

Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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DE.F.7.2.4 - EORTC QLQ-C30 - Definitive deterioration 10 points - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO  
 11-Jan-2022 - Full Analysis Set



Patients still at risk:

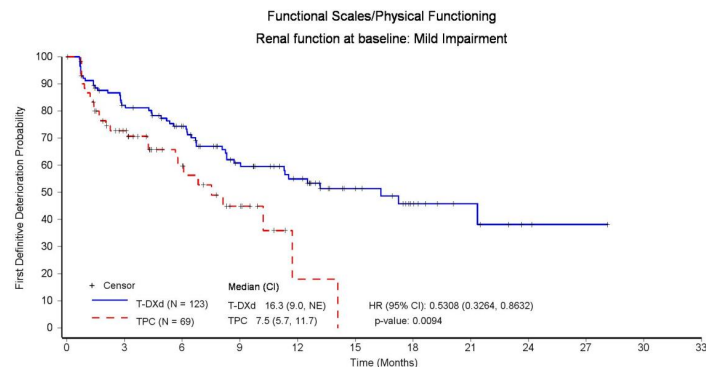
T-DXd (N = 202)	202	147	114	85	47	31	18	12	4	2	1	0
TPC (N = 87)	87	38	18	8	2	1	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:31; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F27C30.rtf

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 Data Intelligence – Evidence Generation  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 123)	123	88	72	48	35	21	11	6	2	1	0	0
TPC (N = 69)	69	36	20	9	1	0	0	0	0	0	0	0

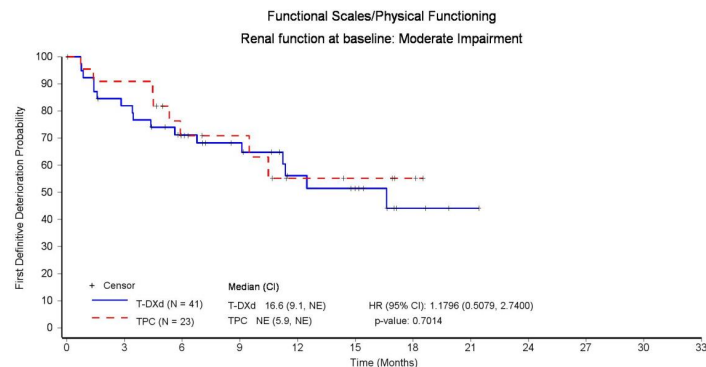
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:31; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F27C30.rtf



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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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Patients still at risk:

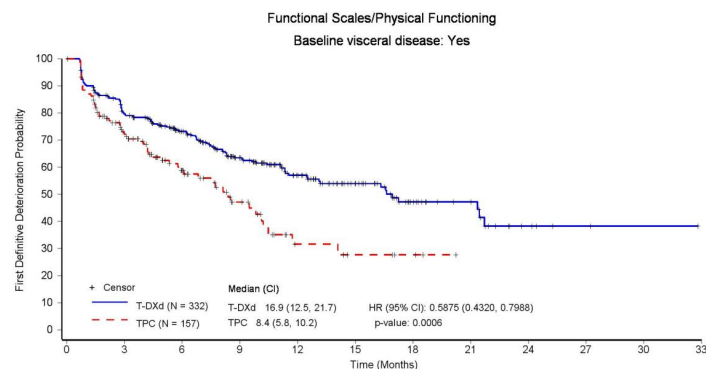
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 41)	41	31	24	20	12	9	3	1	0	0	0	0
TPC (N = 23)	23	20	12	9	5	4	2	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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Patients still at risk:

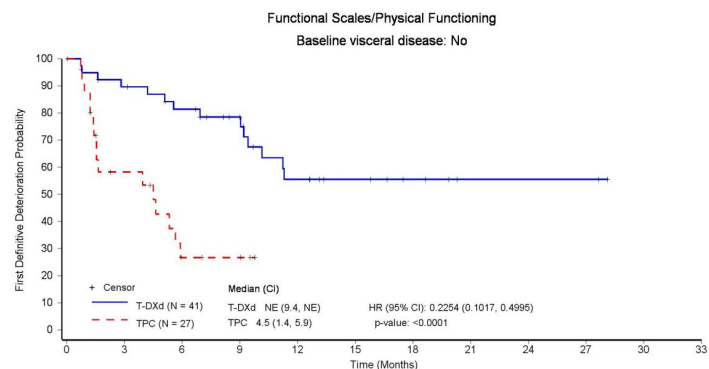
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 332)	332	236	183	132	82	52	27	18	5	2	1	0
TPC (N = 157)	157	84	46	23	8	5	3	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:31; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F27C30.rtf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.7.2.4 - EORTC QLQ-C30 - Definitive deterioration 10 points - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO  
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Patients still at risk:

T-DXd (N = 41)	41	34	29	23	14	10	6	2	2	2	0	0
TPC (N = 27)	27	12	4	3	0	0	0	0	0	0	0	0

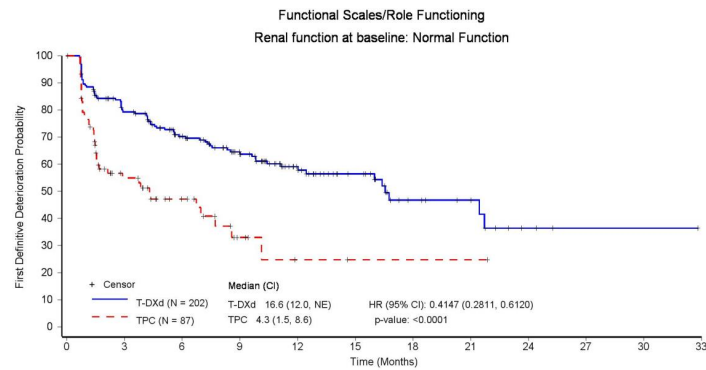
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)

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 Final

DE.F.7.2.4 - EORTC QLQ-C30 - Definitive deterioration 10 points - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO  
 11-Jan-2022 - Full Analysis Set



Patients still at risk:

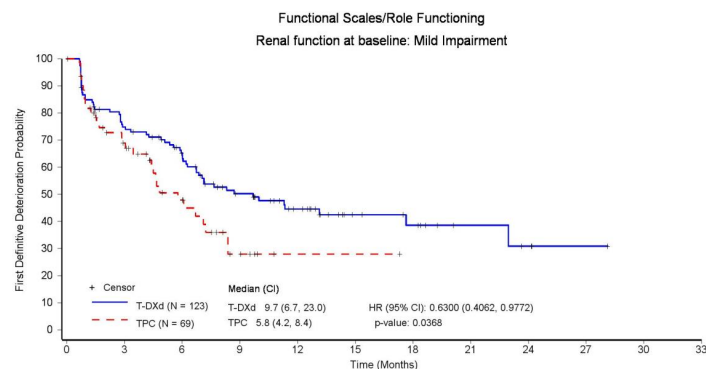
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 202)	202	141	107	79	46	30	14	10	3	1	1	0
TPC (N = 87)	87	31	17	6	2	1	1	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:31; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F27C30.rtf

Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.7.2.4 - EORTC QLQ-C30 - Definitive deterioration 10 points - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO  
 11-Jan-2022 - Full Analysis Set

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Patients still at risk:

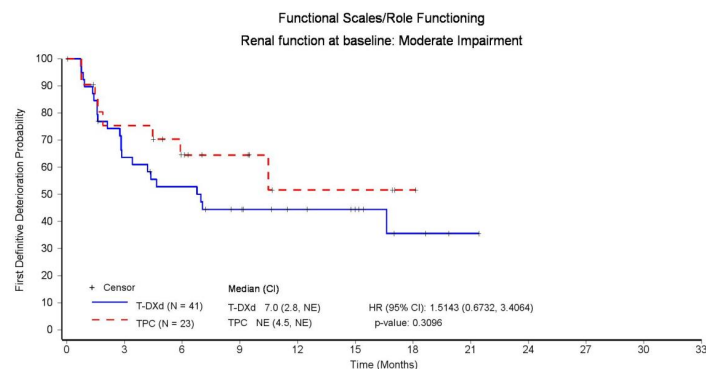
T-DXd (N = 123)	123	81	64	41	27	13	10	5	3	1	0	0
TPC (N = 69)	69	35	18	6	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:31; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F27C30.rtf

Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.7.2.4 - EORTC QLQ-C30 - Definitive deterioration 10 points - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO  
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Patients still at risk:

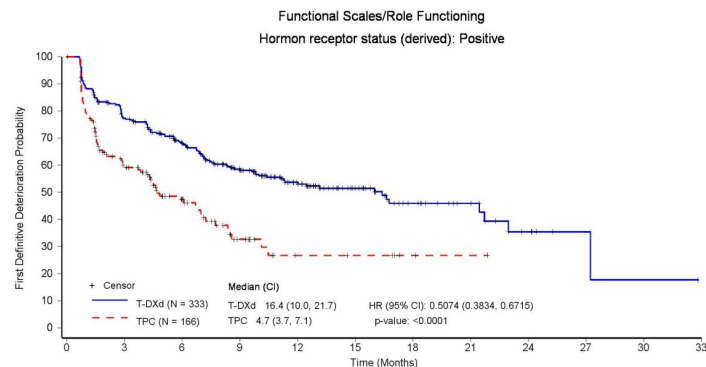
T-DXd (N = 41)	41	24	19	14	10	7	3	1	0	0	0	0
TPC (N = 23)	23	15	10	7	3	3	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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Patients still at risk:

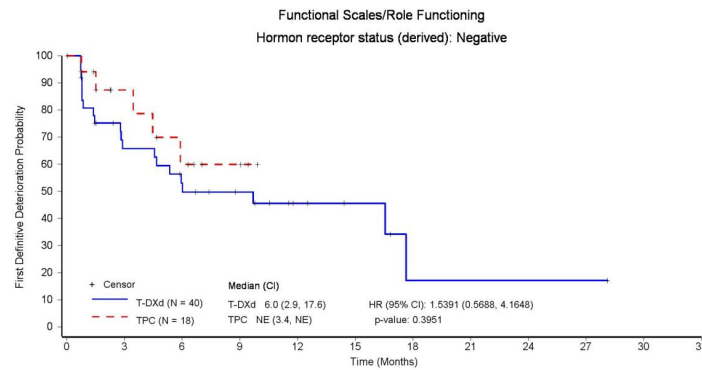
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 333)	333	230	177	125	79	47	27	16	6	2	1	0
TPC (N = 166)	166	73	39	16	6	5	2	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:31; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F27C30.rtf

Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 40)	40	21	16	12	6	4	1	1	1	1	0	0
TPC (N = 18)	18	10	6	3	0	0	0	0	0	0	0	0

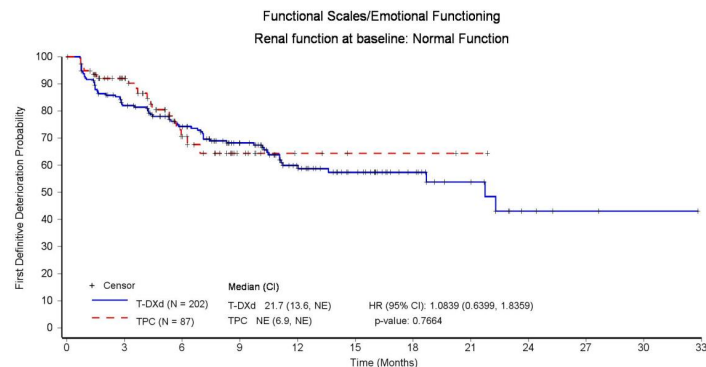
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
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Patients still at risk:

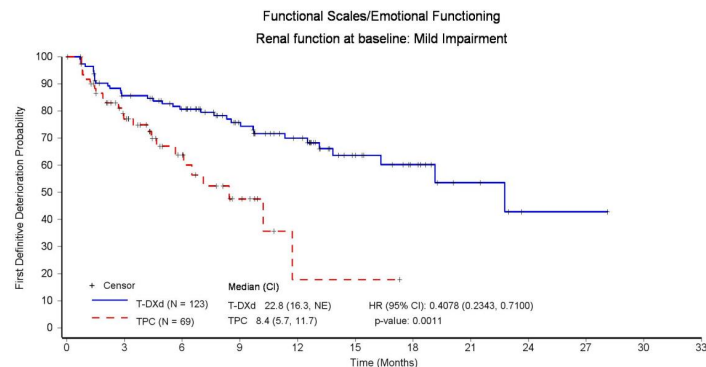
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 202)	202	149	116	87	52	36	21	12	4	2	1	0
TPC (N = 87)	87	53	26	10	4	2	2	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

T-DXd (N = 123)	123	92	79	56	42	22	13	6	1	1	0	0
TPC (N = 69)	69	38	19	8	1	1	0	0	0	0	0	0

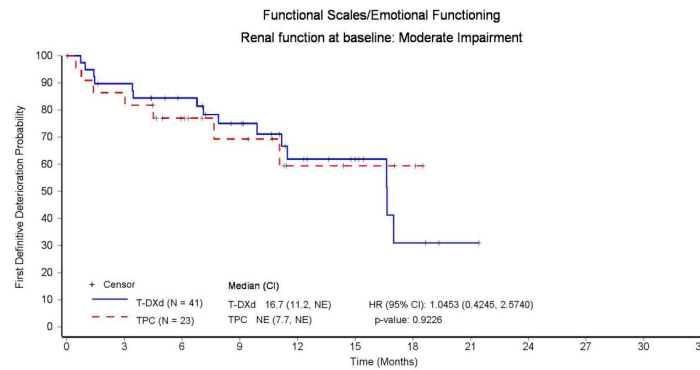
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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DE.F.7.2.4 - EORTC QLQ-C30 - Definitive deterioration 10 points - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO  
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Patients still at risk:

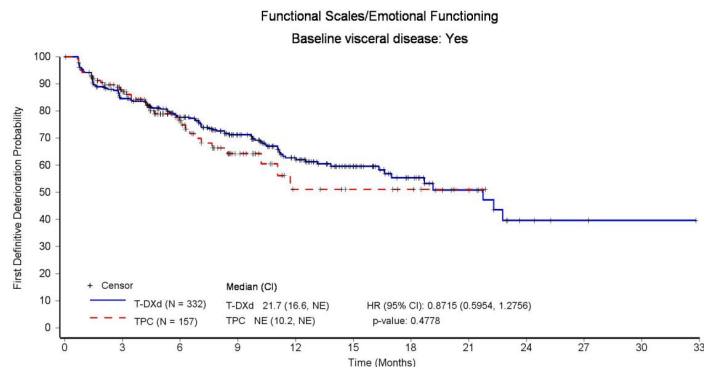
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 41)	41	34	28	22	13	8	3	1	0	0	0	0
TPC (N = 23)	23	19	13	9	4	3	2	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

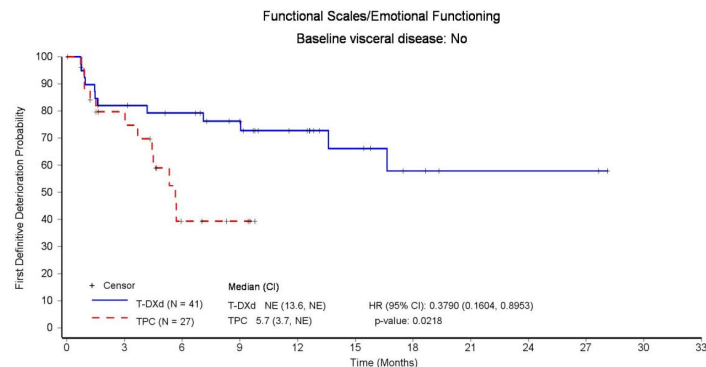
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 332)	332	249	198	145	93	57	33	18	4	2	1	0
TPC (N = 157)	157	98	55	24	9	6	4	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:31; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F27C30.rtf

Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
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Patients still at risk:

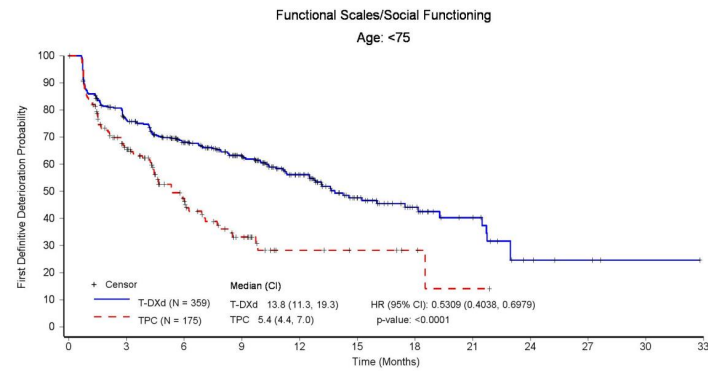
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 41)	41	31	28	23	16	10	5	2	2	2	0	0
TPC (N = 27)	27	16	5	3	0	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:31; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F27C30.rtf

Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
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Patients still at risk:

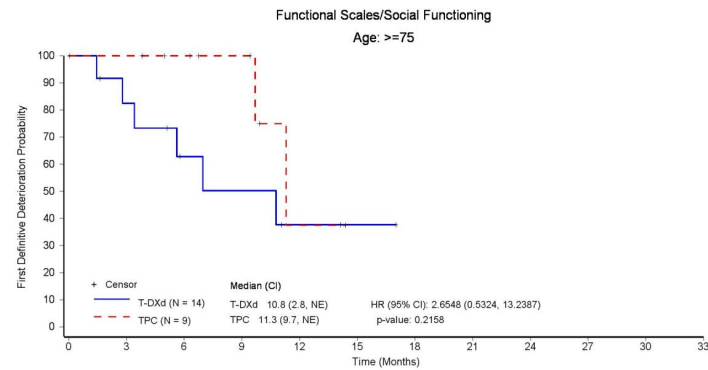
T-DXd (N = 359)	359	242	186	142	90	49	29	16	5	3	1	0
TPC (N = 175)	175	88	43	20	7	5	3	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:31; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F27C30.rtf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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Patients still at risk:

T-DXd (N = 14)	14	9	5	4	2	1	0	0	0	0	0	0
TPC (N = 9)	9	9	7	5	1	0	0	0	0	0	0	0

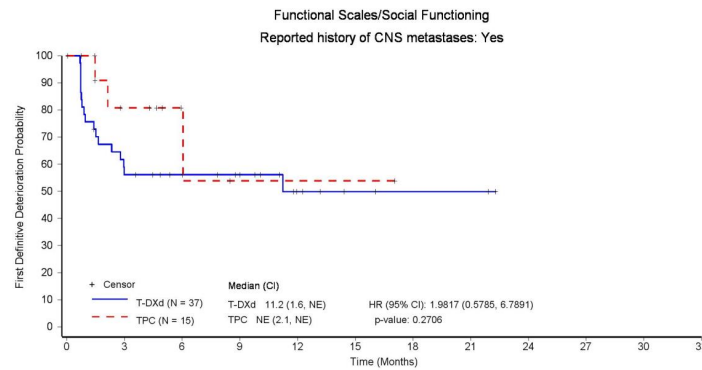
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:31; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F27C30.rtf

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 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 37)	37	20	16	13	6	3	2	2	0	0	0	0
TPC (N = 15)	15	7	3	1	1	1	0	0	0	0	0	0

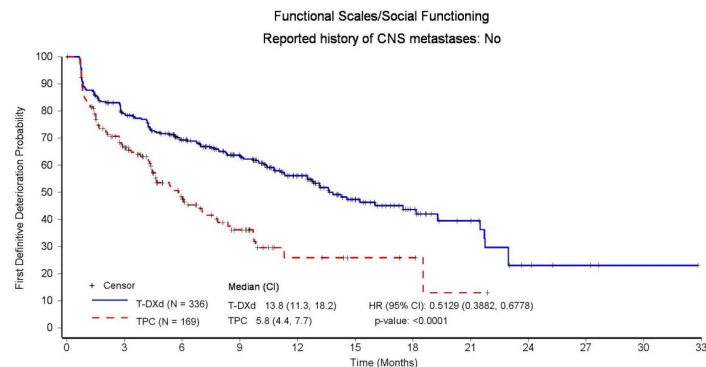
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:31; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F27C30.rtf



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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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Patients still at risk:

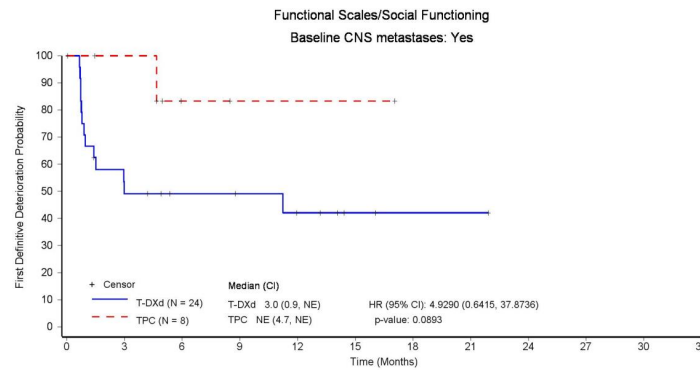
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 336)	336	231	175	133	86	47	27	14	5	3	1	0
TPC (N = 169)	169	90	47	24	7	4	3	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:31; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F27C30.rtf

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 Data Intelligence – Evidence Generation  
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 Statistical analyses for AMNOG (HTA Germany)  
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Patients still at risk:

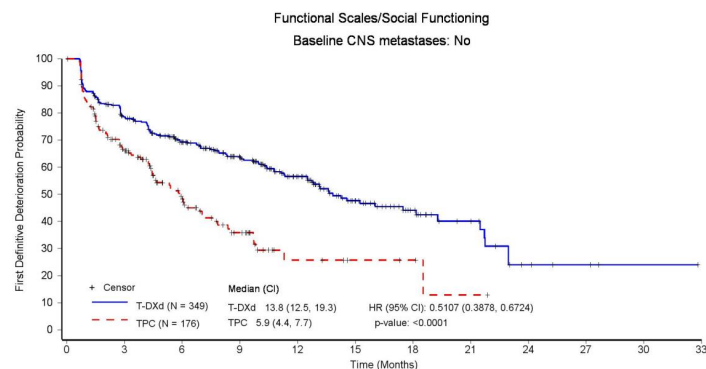
T-DXd (N = 24)	24	11	8	7	5	2	1	1	0	0	0	0
TPC (N = 8)	8	6	2	1	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:31; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F27C30.rtf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 349)	349	240	183	139	87	48	28	15	5	3	1	0
TPC (N = 176)	176	91	48	24	7	4	3	1	0	0	0	0

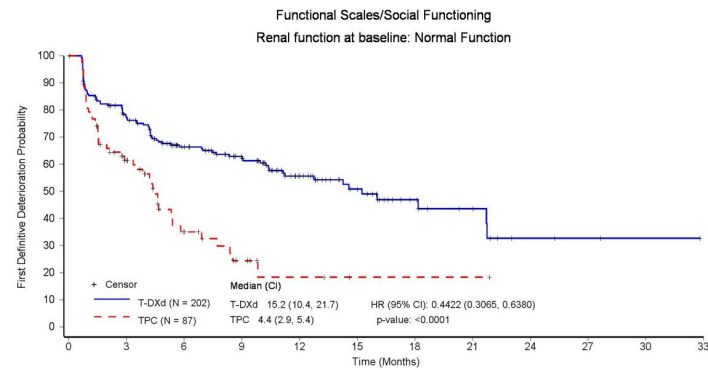
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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Patients still at risk:

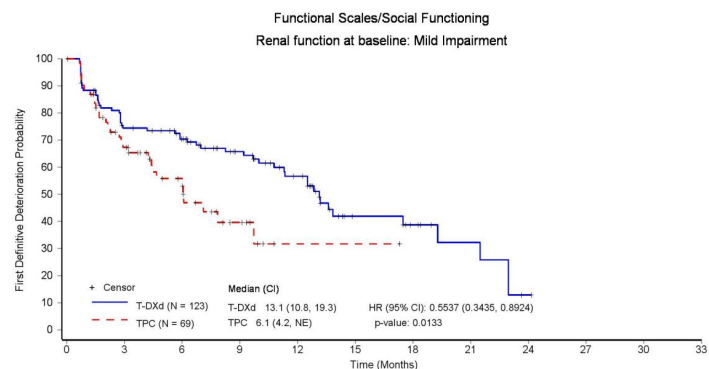
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 202)	202	140	102	80	46	29	15	9	3	2	1	0
TPC (N = 87)	87	39	16	7	3	1	1	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:31; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F27C30.rtf

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Patients still at risk:

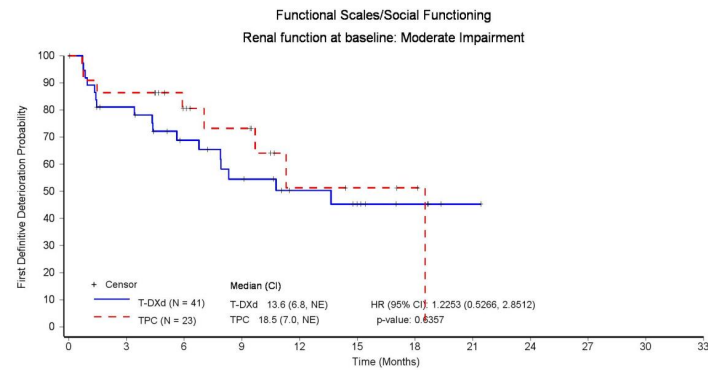
T-DXd (N = 123)	123	79	67	49	34	13	9	5	1	0	0	0
TPC (N = 69)	69	36	20	8	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:31; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F27C30.rtf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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Patients still at risk:

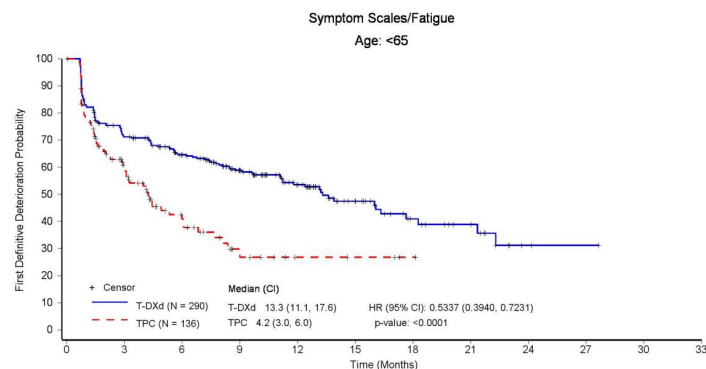
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 41)	41	28	20	15	10	7	4	1	0	0	0	0
TPC (N = 23)	23	19	13	10	4	3	2	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:31; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F27C30.rtf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 290)	290	185	146	109	68	37	20	13	2	1	0	0
TPC (N = 136)	136	56	26	10	4	3	1	0	0	0	0	0

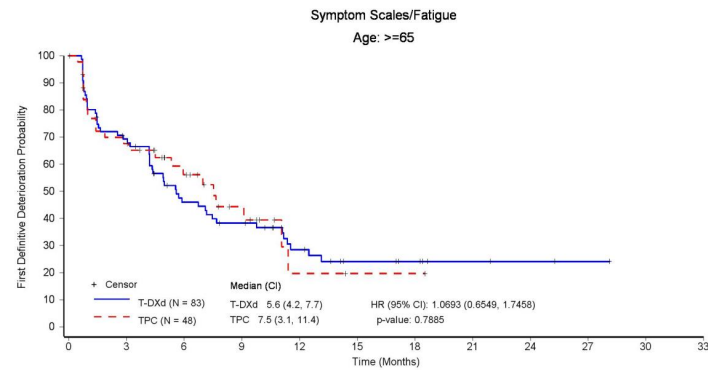
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:31; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F27C30.rtf

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DE.F.7.2.4 - EORTC QLQ-C30 - Definitive deterioration 10 points - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO  
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Patients still at risk:

T-DXd (N = 83)	83	50	30	24	14	8	6	3	2	1	0	0
TPC (N = 48)	48	29	18	9	2	1	1	0	0	0	0	0

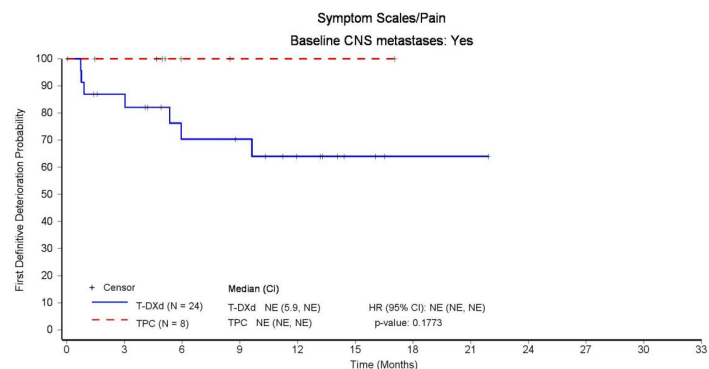
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
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Patients still at risk:

T-DXd (N = 24)	24	18	12	11	7	3	1	1	0	0	0	0
TPC (N = 8)	8	6	2	1	1	1	0	0	0	0	0	0

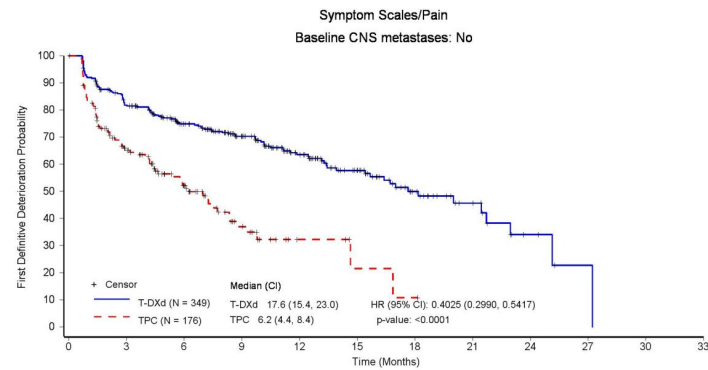
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:31; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F27C30.rtf

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DE.F.7.2.4 - EORTC QLQ-C30 - Definitive deterioration 10 points - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO  
 11-Jan-2022 - Full Analysis Set



Patients still at risk:

T-DXd (N = 349)	349	253	196	148	92	56	31	15	4	1	0	0
TPC (N = 176)	176	85	47	19	5	2	1	0	0	0	0	0

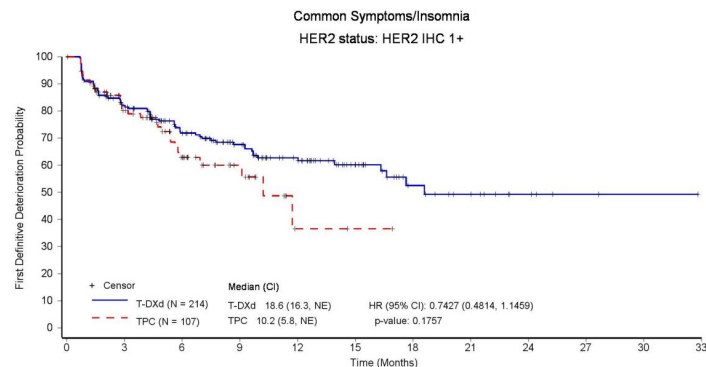
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:31; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F27C30.rtf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 214)	214	151	112	85	60	33	16	11	5	2	1	0
TPC (N = 107)	107	58	31	14	2	1	0	0	0	0	0	0

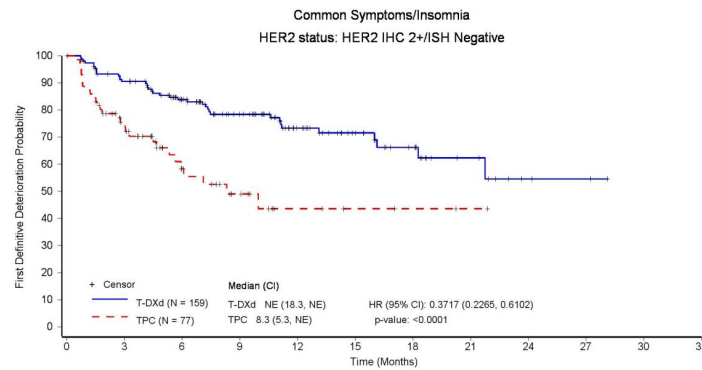
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.7.2.4 - EORTC QLQ-C30 - Definitive deterioration 10 points - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO  
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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 159)	159	131	101	76	46	31	20	9	3	2	0	0
TPC (N = 77)	77	45	21	12	5	3	2	1	0	0	0	0

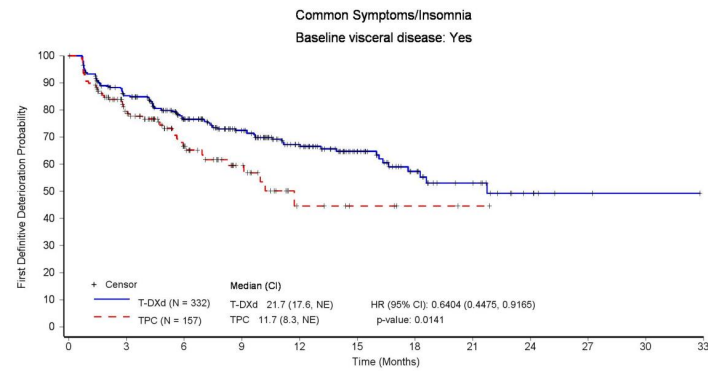
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.7.2.4 - EORTC QLQ-C30 - Definitive deterioration 10 points - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO  
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Patients still at risk:

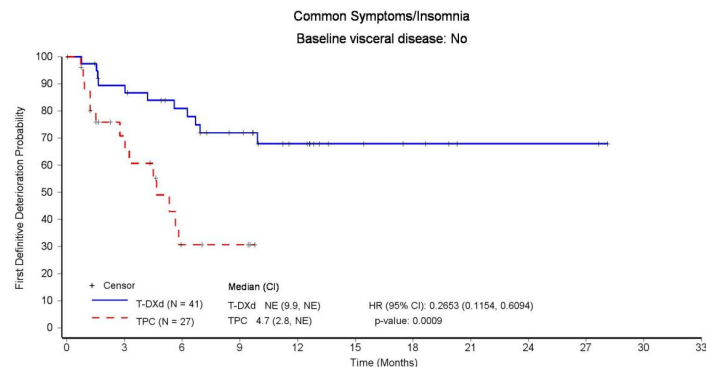
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 332)	332	249	186	140	92	56	31	18	6	2	1	0
TPC (N = 157)	157	89	48	23	7	4	2	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 41)	41	33	27	21	14	8	5	2	2	2	0	0
TPC (N = 27)	27	14	4	3	0	0	0	0	0	0	0	0

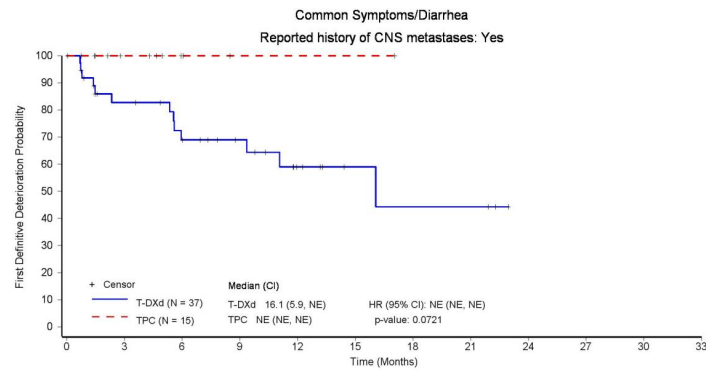
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.7.2.4 - EORTC QLQ-C30 - Definitive deterioration 10 points - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO  
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Patients still at risk:

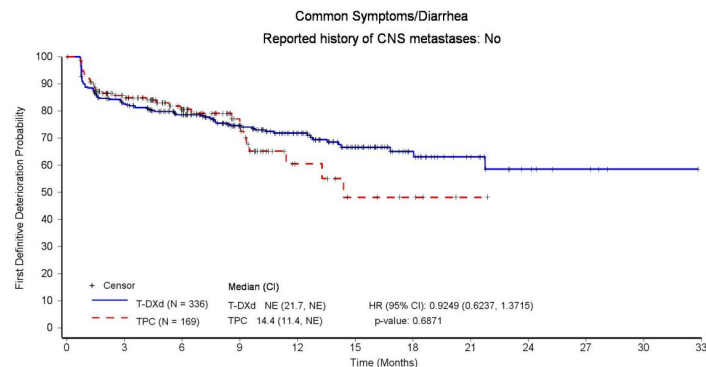
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 37)	37	26	20	15	8	4	3	3	0	0	0	0
TPC (N = 15)	15	8	3	1	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:31; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F27C30.rtf

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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 336)	336	243	199	147	101	61	33	18	7	4	1	0
TPC (N = 169)	169	104	63	34	11	6	4	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:31; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F27C30.rtf



**Anhang 4-G 3.4: EORTC QLQ-BR45 (MID 15 Punkte)**

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DE.T.3.9.1 - EORTC QLQ-BR45 - First deterioration - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Functional Scales/Body Image

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	152 (40.8)	84 (45.7)	
Number of subjects censored, n (%)	221 (59.2)	100 (54.3)	
Median time to first event (months) [a]	13.8	5.1	
95% Confidence Interval	[9.7, NE]	[3.0, 9.8]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.6386
95% Confidence Interval			[0.4863, 0.8385]
p-value			0.0012
Stratified log-rank p-value [c]			0.0011

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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 Run date: 15SEP2022 – 12:16; Program name: T3\_EQ5D\_FD\_1\_FAS.sas; Output name: T3\_EORTCBR45\_FD\_1\_FAS.rtf

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Functional Scales/Sexual Functioning

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	78 (20.9)	34 (18.5)	
Number of subjects censored, n (%)	295 (79.1)	150 (81.5)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.9025 [0.6004, 1.3566] 0.6217
Stratified log-rank p-value [c]			0.6117

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Functional Scales/Sexual Enjoyment

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	33 (8.8)	8 (4.3)	
Number of subjects censored, n (%)	340 (91.2)	176 (95.7)	
Median time to first event (months) [a]	11.2	12.0	
95% Confidence Interval	[4.3, NE]	[NE, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			2.1284
95% Confidence Interval			[0.8626, 5.2516]
p-value			0.1012
Stratified log-rank p-value [c]			0.0943

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 15SEP2022 – 12:16; Program name: T3\_EQ5D\_FD\_1\_FAS.sas; Output name: T3\_EORTCBR45\_FD\_1\_FAS.rtf

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Functional Scales/Future Perspective

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	131 (35.1)	58 (31.5)	
Number of subjects censored, n (%)	242 (64.9)	126 (68.5)	
Median time to first event (months) [a]	17.3	NE	
95% Confidence Interval	[14.9, NE]	[7.7, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.8821
95% Confidence Interval			[0.6433, 1.2095]
p-value			0.4360
Stratified log-rank p-value [c]			0.4392

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Symptom Scales/Systemic Therapy Side Effects

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	161 (43.2)	79 (42.9)	
Number of subjects censored, n (%)	212 (56.8)	105 (57.1)	
Median time to first event (months) [a]	10.3	5.9	
95% Confidence Interval	[6.7, NE]	[4.2, 15.8]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.7733
95% Confidence Interval			[0.5884, 1.0164]
p-value			0.0653
Stratified log-rank p-value [c]			0.0615

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Symptom Scales/Breast Symptoms

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	97 (26.0)	37 (20.1)	
Number of subjects censored, n (%)	276 (74.0)	147 (79.9)	
Median time to first event (months) [a] 95% Confidence Interval	NE [20.3, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.9334 [0.6336, 1.3751] 0.7274
Stratified log-rank p-value [c]			0.7331

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Symptom Scales/Arm Symptoms

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	102 (27.3)	51 (27.7)	
Number of subjects censored, n (%)	271 (72.7)	133 (72.3)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [7.0, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.6386 [0.4523, 0.9018] 0.0109
Stratified log-rank p-value [c]			0.0103

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Symptom Scales/Upset by Hair Loss

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	42 (11.3)	16 (8.7)	
Number of subjects censored, n (%)	331 (88.7)	168 (91.3)	
Median time to first event (months) [a]	7.4	NE	
95% Confidence Interval	[2.9, NE]	[1.2, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.8114
95% Confidence Interval			[0.4293, 1.5336]
p-value			0.5199
Stratified log-rank p-value [c]			0.5325

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.5753
HER2 IHC 1+	214	88 (41.1)	126 (58.9)	13.9 (8.3, NE)	107	47 (43.9)	60 (56.1)	5.9 (2.8, 16.9)	0.6687 (0.4673, 0.9570)	0.0272
HER2 IHC 2+/ISH Negative	159	64 (40.3)	95 (59.7)	13.8 (7.5, NE)	77	37 (48.1)	40 (51.9)	4.2 (2.0, NE)	0.5693 (0.3778, 0.8579)	0.0065

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.1760
1	221	99 (44.8)	122 (55.2)	10.6 (6.3, 20.1)	100	48 (48.0)	52 (52.0)	5.4 (2.8, 16.9)	0.7325 (0.5175, 1.0368) 0.0791	0.0789
>=2	151	53 (35.1)	98 (64.9)	NE (10.5, NE)	83	36 (43.4)	47 (56.6)	4.4 (2.0, NE)	0.5044 (0.3279, 0.7759) 0.0018	0.0016

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Functional Scales/Body Image

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Prior CDK4/6											0.8255
Yes	235	92 (39.1)	143 (60.9)	20.1 (8.3, NE)	118	50 (42.4)	68 (57.6)	5.1 (2.9, NE)	0.6755 (0.4774, 0.9557) 0.0267	0.0256	
No	98	46 (46.9)	52 (53.1)	12.5 (7.5, NE)	48	26 (54.2)	22 (45.8)	4.3 (2.1, 9.8)	0.5880 (0.3610, 0.9577) 0.0329	0.0314	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Functional Scales/Body Image

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											0.0127
<65	290	115 (39.7)	175 (60.3)	13.9 (9.7, NE)	136	68 (50.0)	68 (50.0)	4.2 (2.0, 6.1)	0.5112 (0.3770, 0.6931) <0.0001	<0.0001	
>=65	83	37 (44.6)	46 (55.4)	10.8 (4.2, NE)	48	16 (33.3)	32 (66.7)	16.9 (4.2, NE)	1.1733 (0.6507, 2.1157) 0.5952	0.5887	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Age											
<75	359	149 (41.5)	210 (58.5)	12.8 (8.9, NE)	175	80 (45.7)	95 (54.3)	4.5 (2.9, 8.6)	0.6293 (0.4779, 0.8286)	0.0010	0.5980
>=75	14	3 (21.4)	11 (78.6)	NE (7.0, NE)	9	4 (44.4)	5 (55.6)	16.9 (0.7, 16.9)	0.4745 (0.1053, 2.1372)	0.3208	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.1917
White	176	60 (34.1)	116 (65.9)	NE (10.8, NE)	91	40 (44.0)	51 (56.0)	5.1 (2.8, NE)	0.5342 (0.3561, 0.8013) 0.0024	0.0022	
Non-White	197	92 (46.7)	105 (53.3)	9.7 (7.0, 20.1)	92	43 (46.7)	49 (53.3)	5.9 (2.1, 9.8)	0.7313 (0.5078, 1.0534) 0.0929	0.0923	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.5537
Asia	147	76 (51.7)	71 (48.3)	8.9 (5.6, 16.3)	66	34 (51.5)	32 (48.5)	5.4 (1.7, 9.8)	0.7143 (0.4752, 1.0737) 0.1056	0.1051	
North America	60	15 (25.0)	45 (75.0)	NE (8.3, NE)	33	11 (33.3)	22 (66.7)	4.5 (1.7, NE)	0.4857 (0.2181, 1.0817) 0.0771	0.0706	
Europe + Israel	166	61 (36.7)	105 (63.3)	NE (9.7, NE)	85	39 (45.9)	46 (54.1)	5.1 (2.8, NE)	0.5963 (0.3976, 0.8943) 0.0124	0.0117	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
ECOG PS											0.2432
0	200	84 (42.0)	116 (58.0)	14.1 (8.3, NE)	105	50 (47.6)	55 (52.4)	3.9 (1.7, 9.8)	0.5529 (0.3879, 0.7882) 0.0011	0.0009	
1	173	68 (39.3)	105 (60.7)	12.5 (8.3, NE)	79	34 (43.0)	45 (57.0)	6.1 (4.2, NE)	0.7466 (0.4926, 1.1313) 0.1682	0.1652	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.8619
0	60	24 (40.0)	36 (60.0)	12.5 (4.7, NE)	34	16 (47.1)	18 (52.9)	3.9 (1.4, NE)	0.5072 (0.2645, 0.9726) 0.0410	0.0376	
1	108	44 (40.7)	64 (59.3)	12.5 (5.9, NE)	51	24 (47.1)	27 (52.9)	6.1 (1.5, NE)	0.6767 (0.4103, 1.1161) 0.1261	0.1255	
2	115	43 (37.4)	72 (62.6)	NE (8.3, NE)	54	24 (44.4)	30 (55.6)	5.1 (2.1, NE)	0.5917 (0.3557, 0.9842) 0.0432	0.0414	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	41 (45.6)	49 (54.4)	12.8 (7.2, NE)	45	20 (44.4)	25 (55.6)	4.4 (2.8, NE)	0.7114 (0.4135, 1.2239) 0.2186	0.2166

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.9652
PD	174	64 (36.8)	110 (63.2)	16.3 (9.6, NE)	85	34 (40.0)	51 (60.0)	5.9 (2.9, NE)	0.6438 (0.4225, 0.9811) 0.0405	0.0392	
PR	48	25 (52.1)	23 (47.9)	7.4 (4.2, NE)	22	9 (40.9)	13 (59.1)	4.3 (1.0, NE)	0.7177 (0.3331, 1.5461) 0.3969	0.3993	
SD	82	36 (43.9)	46 (56.1)	12.5 (3.1, NE)	55	29 (52.7)	26 (47.3)	5.9 (1.7, 16.9)	0.6905 (0.4218, 1.1304) 0.1409	0.1400	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.0328
Yes	37	18 (48.6)	19 (51.4)	8.8 (2.8, NE)	15	3 (20.0)	12 (80.0)	NE (2.9, NE)	1.8357 (0.5371, 6.2745) 0.3327	0.3262	
No	336	134 (39.9)	202 (60.1)	13.9 (10.4, NE)	169	81 (47.9)	88 (52.1)	4.4 (2.8, 8.6)	0.5807 (0.4393, 0.7675) 0.0001	0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.2892
Yes	24	12 (50.0)	12 (50.0)	8.8 (3.0, NE)	8	3 (37.5)	5 (62.5)	5.9 (1.4, NE)	1.0117 (0.2834, 3.6122) 0.9857	0.9897	
No	349	140 (40.1)	209 (59.9)	13.9 (10.4, NE)	176	81 (46.0)	95 (54.0)	5.1 (2.8, 9.8)	0.6122 (0.4643, 0.8074) 0.0005	0.0005	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.1608
Normal Function	202	84 (41.6)	118 (58.4)	12.5 (7.4, NE)	87	47 (54.0)	40 (46.0)	2.8 (1.4, 5.9)	0.4723 (0.3286, 0.6789) 0.0001	<0.0001	
Mild Impairment	123	48 (39.0)	75 (61.0)	16.3 (9.7, NE)	69	28 (40.6)	41 (59.4)	4.3 (2.8, NE)	0.6339 (0.3928, 1.0230) 0.0619	0.0612	
Moderate Impairment	41	15 (36.6)	26 (63.4)	NE (4.2, NE)	23	8 (34.8)	15 (65.2)	16.9 (4.5, NE)	1.1196 (0.4734, 2.6482) 0.7970	0.7964	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.5077
Normal Function	170	73 (42.9)	97 (57.1)	13.8 (7.4, NE)	98	50 (51.0)	48 (49.0)	4.2 (1.7, 9.8)	0.5751 (0.3996, 0.8277) 0.0029	0.0026	
Mild Impairment	195	76 (39.0)	119 (61.0)	14.1 (8.8, NE)	84	34 (40.5)	50 (59.5)	6.5 (2.7, NE)	0.6750 (0.4485, 1.0159) 0.0595	0.0609	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.0481
Yes	332	135 (40.7)	197 (59.3)	13.8 (9.6, NE)	157	66 (42.0)	91 (58.0)	6.1 (3.9, NE)	0.7062 (0.5250, 0.9500) 0.0215	0.0213	
No	41	17 (41.5)	24 (58.5)	12.8 (3.0, NE)	27	18 (66.7)	9 (33.3)	1.7 (0.9, 4.5)	0.3395 (0.1672, 0.6894) 0.0028	0.0017	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (IXRS)											0.1420
Positive	331	138 (41.7)	193 (58.3)	13.8 (9.6, NE)	163	72 (44.2)	91 (55.8)	5.4 (3.9, 9.8)	0.6773 (0.5080, 0.9031) 0.0080	0.0077	
Negative	42	14 (33.3)	28 (66.7)	12.5 (5.0, NE)	21	12 (57.1)	9 (42.9)	1.5 (0.9, NE)	0.3490 (0.1573, 0.7742) 0.0096	0.0069	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.6002
Positive	333	138 (41.4)	195 (58.6)	13.8 (9.6, NE)	166	76 (45.8)	90 (54.2)	5.1 (3.0, 9.8)	0.6475 (0.4880, 0.8591) 0.0026	0.0024	
Negative	40	14 (35.0)	26 (65.0)	12.5 (5.0, NE)	18	8 (44.4)	10 (55.6)	5.9 (0.9, NE)	0.4738 (0.1939, 1.1574) 0.1012	0.0928	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0526
HER2 IHC 1+	214	45 (21.0)	169 (79.0)	NE (NE, NE)	107	14 (13.1)	93 (86.9)	NE (NE, NE)	1.3706 (0.7508, 2.5023) 0.3046	0.3045	
HER2 IHC 2+/ISH Negative	159	33 (20.8)	126 (79.2)	NE (NE, NE)	77	20 (26.0)	57 (74.0)	NE (NE, NE)	0.6129 (0.3501, 1.0732) 0.0868	0.0842	

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[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.1182
1	221	52 (23.5)	169 (76.5)	NE (NE, NE)	100	16 (16.0)	84 (84.0)	NE (NE, NE)	1.2182 (0.6946, 2.1365) 0.4912	0.4869	
>=2	151	26 (17.2)	125 (82.8)	NE (NE, NE)	83	18 (21.7)	65 (78.3)	NE (NE, NE)	0.6458 (0.3521, 1.1845) 0.1577	0.1537	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.2828
Yes	235	51 (21.7)	184 (78.3)	NE (NE, NE)	118	24 (20.3)	94 (79.7)	NE (NE, NE)	0.7955 (0.4873, 1.2987) 0.3603	0.3571	
No	98	20 (20.4)	78 (79.6)	NE (NE, NE)	48	6 (12.5)	42 (87.5)	NE (NE, NE)	1.4732 (0.5914, 3.6701) 0.4054	0.4040	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3832
<65	290	66 (22.8)	224 (77.2)	NE (NE, NE)	136	29 (21.3)	107 (78.7)	NE (NE, NE)	0.8152 (0.5251, 1.2654) 0.3623	0.3612	
>=65	83	12 (14.5)	71 (85.5)	NE (NE, NE)	48	5 (10.4)	43 (89.6)	NE (NE, NE)	1.3707 (0.4825, 3.8942) 0.5539	0.5559	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9276
<75	359	77 (21.4)	282 (78.6)	NE (NE, NE)	175	33 (18.9)	142 (81.1)	NE (NE, NE)	0.9042 (0.5999, 1.3629)	0.6291	
>=75	14	1 (7.1)	13 (92.9)	NE (NE, NE)	9	1 (11.1)	8 (88.9)	NE (0.7, NE)	0.7071 (0.0442, 11.3185)	0.8055	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.0543
White	176	43 (24.4)	133 (75.6)	NE (NE, NE)	91	24 (26.4)	67 (73.6)	NE (4.5, NE)	0.6805 (0.4110, 1.1265) 0.1344	0.1316	
Non-White	197	35 (17.8)	162 (82.2)	NE (NE, NE)	92	9 (9.8)	83 (90.2)	NE (NE, NE)	1.6009 (0.7680, 3.3372) 0.2092	0.2024	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.3323
Asia	147	21 (14.3)	126 (85.7)	NE (NE, NE)	66	5 (7.6)	61 (92.4)	NE (NE, NE)	1.6515 (0.6213, 4.3896) 0.3145	0.3049	
North America	60	10 (16.7)	50 (83.3)	NE (NE, NE)	33	7 (21.2)	26 (78.8)	NE (2.7, NE)	0.6275 (0.2377, 1.6567) 0.3469	0.3383	
Europe + Israel	166	47 (28.3)	119 (71.7)	NE (NE, NE)	85	22 (25.9)	63 (74.1)	NE (7.0, NE)	0.8736 (0.5247, 1.4546) 0.6035	0.6023	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.4926
0	200	48 (24.0)	152 (76.0)	NE (NE, NE)	105	23 (21.9)	82 (78.1)	NE (NE, NE)	0.8259 (0.5010, 1.3614) 0.4531	0.4584	
1	173	30 (17.3)	143 (82.7)	NE (NE, NE)	79	11 (13.9)	68 (86.1)	NE (NE, NE)	1.1323 (0.5661, 2.2651) 0.7253	0.7288	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.0657
0	60	12 (20.0)	48 (80.0)	NE (NE, NE)	34	8 (23.5)	26 (76.5)	NE (3.4, NE)	0.6883 (0.2811, 1.6853) 0.4136	0.4123	
1	108	27 (25.0)	81 (75.0)	NE (NE, NE)	51	5 (9.8)	46 (90.2)	NE (NE, NE)	2.4837 (0.9556, 6.4554) 0.0619	0.0534	
2	115	23 (20.0)	92 (80.0)	NE (NE, NE)	54	12 (22.2)	42 (77.8)	NE (7.0, NE)	0.6724 (0.3315, 1.3640) 0.2714	0.2605	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	16 (17.8)	74 (82.2)	NE (NE, NE)	45	9 (20.0)	36 (80.0)	NE (NE, NE)	0.6719 (0.2949, 1.5311) 0.3440	0.3402

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.1029
PD	174	44 (25.3)	130 (74.7)	NE (NE, NE)	85	19 (22.4)	66 (77.6)	NE (NE, NE)	0.9156 (0.5337, 1.5709) 0.7489	0.7493	
PR	48	5 (10.4)	43 (89.6)	NE (NE, NE)	22	5 (22.7)	17 (77.3)	NE (0.9, NE)	0.2249 (0.0627, 0.8074) 0.0221	0.0129	
SD	82	14 (17.1)	68 (82.9)	NE (NE, NE)	55	6 (10.9)	49 (89.1)	NE (NE, NE)	1.4752 (0.5655, 3.8483) 0.4268	0.4246	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.7592
Yes	37	9 (24.3)	28 (75.7)	NE (NE, NE)	15	3 (20.0)	12 (80.0)	NE (0.9, NE)	0.7649 (0.2056, 2.8453) 0.6893	0.6909	
No	336	69 (20.5)	267 (79.5)	NE (NE, NE)	169	31 (18.3)	138 (81.7)	NE (NE, NE)	0.9349 (0.6107, 1.4313) 0.7567	0.7561	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.6686
Yes	24	5 (20.8)	19 (79.2)	NE (6.9, NE)	8	2 (25.0)	6 (75.0)	NE (0.9, NE)	0.5557 (0.1016, 3.0388) 0.4979	0.4917	
No	349	73 (20.9)	276 (79.1)	NE (NE, NE)	176	32 (18.2)	144 (81.8)	NE (NE, NE)	0.9476 (0.6242, 1.4386) 0.8005	0.8011	

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[c] Two-sided p-value from unstratified log-rank test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.7109
Normal Function	202	46 (22.8)	156 (77.2)	NE (NE, NE)	87	19 (21.8)	68 (78.2)	NE (NE, NE)	0.7708 (0.4497, 1.3213) 0.3438	0.3418	
Mild Impairment	123	28 (22.8)	95 (77.2)	NE (NE, NE)	69	12 (17.4)	57 (82.6)	NE (NE, NE)	1.0875 (0.5513, 2.1452) 0.8089	0.8126	
Moderate Impairment	41	4 (9.8)	37 (90.2)	NE (NE, NE)	23	2 (8.7)	21 (91.3)	NE (NE, NE)	1.2821 (0.2344, 7.0136) 0.7744	0.7739	

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.5798
Normal Function	170	38 (22.4)	132 (77.6)	NE (NE, NE)	98	22 (22.4)	76 (77.6)	NE (NE, NE)	0.8634 (0.5096, 1.4629)	0.5779	
Mild Impairment	195	40 (20.5)	155 (79.5)	NE (NE, NE)	84	12 (14.3)	72 (85.7)	NE (NE, NE)	1.0378 (0.5418, 1.9878)	0.9073	

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.6982
Yes	332	65 (19.6)	267 (80.4)	NE (NE, NE)	157	27 (17.2)	130 (82.8)	NE (NE, NE)	0.9166 (0.5840, 1.4386) 0.7050	0.7052	
No	41	13 (31.7)	28 (68.3)	NE (6.9, NE)	27	7 (25.9)	20 (74.1)	NE (4.5, NE)	1.0721 (0.4235, 2.7138) 0.8832	0.8860	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.5573
Positive	331	71 (21.5)	260 (78.5)	NE (NE, NE)	163	29 (17.8)	134 (82.2)	NE (NE, NE)	0.9589 (0.6212, 1.4802) 0.8499	0.8508	
Negative	42	7 (16.7)	35 (83.3)	NE (NE, NE)	21	5 (23.8)	16 (76.2)	NE (3.4, NE)	0.7156 (0.2271, 2.2554) 0.5678	0.5667	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.6707
Positive	333	71 (21.3)	262 (78.7)	NE (NE, NE)	166	30 (18.1)	136 (81.9)	NE (NE, NE)	0.9451 (0.6154, 1.4515) 0.7964	0.7949	
Negative	40	7 (17.5)	33 (82.5)	NE (NE, NE)	18	4 (22.2)	14 (77.8)	NE (1.6, NE)	0.7637 (0.2235, 2.6098) 0.6673	0.6679	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.2742
HER2 IHC 1+	214	16 (7.5)	198 (92.5)	11.2 (1.7, NE)	107	5 (4.7)	102 (95.3)	NE (0.9, NE)	1.1752 (0.4206, 3.2835) 0.7581	0.7556
HER2 IHC 2+/ISH Negative	159	17 (10.7)	142 (89.3)	7.1 (4.2, NE)	77	3 (3.9)	74 (96.1)	12.0 (NE, NE)	2.5097 (0.7331, 8.5918) 0.1428	0.1302

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.6423
1	221	19 (8.6)	202 (91.4)	11.2 (4.3, NE)	100	5 (5.0)	95 (95.0)	12.0 (NE, NE)	1.3228 (0.4875, 3.5893) 0.5828	0.5733
>=2	151	14 (9.3)	137 (90.7)	5.6 (1.7, NE)	83	3 (3.6)	80 (96.4)	NE (2.3, NE)	2.4644 (0.7065, 8.5966) 0.1571	0.1446

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.7542
Yes	235	24 (10.2)	211 (89.8)	12.6 (4.3, NE)	118	4 (3.4)	114 (96.6)	NE (NE, NE)	2.1642 (0.7449, 6.2878) 0.1560	0.1454	
No	98	7 (7.1)	91 (92.9)	11.2 (1.7, NE)	48	2 (4.2)	46 (95.8)	12.0 (0.8, 12.0)	1.4443 (0.2979, 7.0022) 0.6481	0.6401	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7910
<65	290	28 (9.7)	262 (90.3)	11.2 (4.3, NE)	136	7 (5.1)	129 (94.9)	12.0 (NE, NE)	1.5720 (0.6795, 3.6369) 0.2905	0.2887	
>=65	83	5 (6.0)	78 (94.0)	8.4 (1.0, NE)	48	1 (2.1)	47 (97.9)	NE (0.8, NE)	1.7501 (0.1940, 15.7860) 0.6180	0.6134	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											NE
<75	359	32 (8.9)	327 (91.1)	11.2 (4.2, NE)	175	8 (4.6)	167 (95.4)	12.0 (NE, NE)	1.6509 (0.7543, 3.6132) 0.2097	0.2040	
>=75	14	1 (7.1)	13 (92.9)	8.4 (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Race										0.5461
White	176	17 (9.7)	159 (90.3)	12.6 (6.9, NE)	91	4 (4.4)	87 (95.6)	NE (NE, NE)	1.7208 (0.5713, 5.1836)	0.3289
Non-White	197	16 (8.1)	181 (91.9)	4.2 (0.8, NE)	92	4 (4.3)	88 (95.7)	12.0 (0.8, 12.0)	1.2389 (0.4132, 3.7150)	0.6800

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Region										0.1960
Asia	147	8 (5.4)	139 (94.6)	2.9 (0.7, 11.2)	66	1 (1.5)	65 (98.5)	12.0 (NE, NE)	4.1825 (0.5151, 33.9632)	0.1471
North America	60	6 (10.0)	54 (90.0)	NE (2.1, NE)	33	0	33 (100)	NE (NE, NE)	NE (NE, NE)	0.2447
Europe + Israel	166	19 (11.4)	147 (88.6)	12.6 (4.2, NE)	85	7 (8.2)	78 (91.8)	NE (2.8, NE)	1.2381 (0.5143, 2.9803)	0.6296

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.5145
0	200	18 (9.0)	182 (91.0)	12.6 (4.2, NE)	105	6 (5.7)	99 (94.3)	12.0 (NE, NE)	1.3030 (0.5067, 3.3506) 0.5828	0.5809	
1	173	15 (8.7)	158 (91.3)	6.9 (1.4, NE)	79	2 (2.5)	77 (97.5)	NE (2.8, NE)	2.6567 (0.6056, 11.6542) 0.1952	0.1792	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.7729
0	60	5 (8.3)	55 (91.7)	1.7 (0.7, NE)	34	3 (8.8)	31 (91.2)	12.0 (0.9, 12.0)	1.3971 (0.3306, 5.9043) 0.6493	0.6478	
1	108	12 (11.1)	96 (88.9)	5.6 (0.8, NE)	51	3 (5.9)	48 (94.1)	NE (0.8, NE)	1.4892 (0.4183, 5.3015) 0.5388	0.5109	
2	115	13 (11.3)	102 (88.7)	10.5 (3.0, NE)	54	1 (1.9)	53 (98.1)	NE (2.8, NE)	3.7651 (0.4836, 29.3157) 0.2055	0.1746	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	3 (3.3)	87 (96.7)	NE (11.2, NE)	45	1 (2.2)	44 (97.8)	NE (0.5, NE)	1.2902 (0.1167, 14.2652)	0.8349	0.8354

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.1044
PD	174	14 (8.0)	160 (92.0)	NE (4.1, NE)	85	6 (7.1)	79 (92.9)	NE (2.3, NE)	1.1126 (0.4251, 2.9123) 0.8279	0.8281	
PR	48	3 (6.3)	45 (93.8)	3.0 (0.8, NE)	22	0	22 (100)	NE (NE, NE)	NE (NE, NE) 0.9973	0.1362	
SD	82	9 (11.0)	73 (89.0)	4.9 (1.1, NE)	55	1 (1.8)	54 (98.2)	12.0 (NE, NE)	5.2224 (0.6567, 41.5302) 0.1182	0.0814	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.2226
Yes	37	4 (10.8)	33 (89.2)	6.9 (1.4, NE)	15	0	15 (100)	NE (NE, NE)	NE (NE, NE) 0.9977	0.3130	
No	336	29 (8.6)	307 (91.4)	11.2 (4.3, NE)	169	8 (4.7)	161 (95.3)	12.0 (NE, NE)	1.4763 (0.6681, 3.2618) 0.3355	0.3315	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Baseline CNS metastases											NE
Yes	24	1 (4.2)	23 (95.8)	NE (1.6, NE)	8	0	8 (100)	NE (NE, NE)	NE (NE, NE)		
No	349	32 (9.2)	317 (90.8)	8.4 (4.2, NE)	176	8 (4.5)	168 (95.5)	12.0 (NE, NE)	1.6708 (0.7629, 3.6590)	0.1937	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Renal function at baseline										0.5236
Normal Function	202	21 (10.4)	181 (89.6)	12.6 (3.0, NE)	87	6 (6.9)	81 (93.1)	12.0 (2.3, 12.0)	1.2365 (0.4927, 3.1029)	0.6511
Mild Impairment	123	9 (7.3)	114 (92.7)	8.3 (3.5, NE)	69	1 (1.4)	68 (98.6)	NE (NE, NE)	3.9376 (0.4975, 31.1636)	0.1610
Moderate Impairment	41	3 (7.3)	38 (92.7)	8.4 (1.6, 11.2)	23	1 (4.3)	22 (95.7)	NE (0.8, NE)	0.4714 (0.0283, 7.8580)	0.1941

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.0490
Normal Function	170	12 (7.1)	158 (92.9)	NE (4.2, NE)	98	6 (6.1)	92 (93.9)	12.0 (1.8, 12.0)	0.8366 (0.3060, 2.2867) 0.7280	0.7255	
Mild Impairment	195	21 (10.8)	174 (89.2)	6.9 (3.5, NE)	84	2 (2.4)	82 (97.6)	NE (NE, NE)	4.1522 (0.9700, 17.7737) 0.0550	0.0366	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Baseline visceral disease										0.1646
Yes	332	27 (8.1)	305 (91.9)	8.3 (4.2, NE)	157	6 (3.8)	151 (96.2)	12.0 (NE, NE)	2.0668 (0.8479, 5.0380)	0.1103
No	41	6 (14.6)	35 (85.4)	11.2 (0.7, NE)	27	2 (7.4)	25 (92.6)	2.3 (0.9, 2.3)	0.3327 (0.0429, 2.5779)	0.2712

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)										0.9150	
Positive	331	30 (9.1)	301 (90.9)	11.2 (4.4, NE)	163	6 (3.7)	157 (96.3)	12.0 (NE, NE)	1.8191 (0.7507, 4.4082)	0.1770	
Negative	42	3 (7.1)	39 (92.9)	1.3 (0.7, NE)	21	2 (9.5)	19 (90.5)	NE (0.9, NE)	2.1709 (0.3498, 13.4722)	0.3948	

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[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]	
Hormon receptor status (derived)										0.8407	
Positive	333	31 (9.3)	302 (90.7)	11.2 (4.3, NE)	166	6 (3.6)	160 (96.4)	12.0 (NE, NE)	1.9006 (0.7865, 4.5926)	0.1451	
Negative	40	2 (5.0)	38 (95.0)	1.1 (0.7, NE)	18	2 (11.1)	16 (88.9)	2.3 (0.9, NE)	1.4142 (0.1962, 10.1915)	0.7297	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
HER2 status										0.2605
HER2 IHC 1+	214	75 (35.0)	139 (65.0)	17.3 (12.9, NE)	107	29 (27.1)	78 (72.9)	NE (11.1, NE)	0.9774 (0.6327, 1.5098)	0.9184
HER2 IHC 2+/ISH Negative	159	56 (35.2)	103 (64.8)	NE (14.9, NE)	77	29 (37.7)	48 (62.3)	NE (4.4, NE)	0.7119 (0.4527, 1.1194)	0.1399

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[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.3.9.2 - EORTC QLQ-BR45 - First deterioration - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.0576
1	221	80 (36.2)	141 (63.8)	17.3 (12.7, NE)	100	28 (28.0)	72 (72.0)	NE (11.1, NE)	1.1160 (0.7230, 1.7225) 0.6204	0.6189
>=2	151	50 (33.1)	101 (66.9)	NE (13.3, NE)	83	30 (36.1)	53 (63.9)	NE (4.3, NE)	0.5747 (0.3621, 0.9123) 0.0188	0.0176

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.5219
Yes	235	77 (32.8)	158 (67.2)	23.6 (13.3, NE)	118	31 (26.3)	87 (73.7)	NE (NE, NE)	0.9461 (0.6201, 1.4436) 0.7972	0.7972	
No	98	40 (40.8)	58 (59.2)	16.6 (10.0, NE)	48	20 (41.7)	28 (58.3)	11.1 (5.7, NE)	0.7365 (0.4274, 1.2691) 0.2706	0.2693	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3727
<65	290	95 (32.8)	195 (67.2)	23.6 (16.9, NE)	136	41 (30.1)	95 (69.9)	NE (6.1, NE)	0.8165 (0.5640, 1.1818)	0.2830	
>=65	83	36 (43.4)	47 (56.6)	12.9 (8.2, NE)	48	17 (35.4)	31 (64.6)	11.3 (4.4, NE)	0.9888 (0.5509, 1.7747)	0.9702	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5355
<75	359	124 (34.5)	235 (65.5)	23.6 (16.3, NE)	175	54 (30.9)	121 (69.1)	NE (7.1, NE)	0.8495 (0.6150, 1.1735) 0.3225	0.3229	
>=75	14	7 (50.0)	7 (50.0)	13.3 (4.2, NE)	9	4 (44.4)	5 (55.6)	11.3 (0.7, NE)	1.0904 (0.3168, 3.7530) 0.8908	0.8908	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.8664
White	176	47 (26.7)	129 (73.3)	23.6 (23.6, NE)	91	21 (23.1)	70 (76.9)	NE (11.1, NE)	0.8638 (0.5115, 1.4586) 0.5838	0.5847	
Non-White	197	84 (42.6)	113 (57.4)	16.3 (8.3, NE)	92	37 (40.2)	55 (59.8)	7.7 (4.9, NE)	0.8119 (0.5496, 1.1994) 0.2952	0.2942	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.0874
Asia	147	63 (42.9)	84 (57.1)	16.9 (9.6, NE)	66	31 (47.0)	35 (53.0)	7.1 (3.5, NE)	0.6815 (0.4416, 1.0516) 0.0832	0.0818	
North America	60	12 (20.0)	48 (80.0)	NE (NE, NE)	33	9 (27.3)	24 (72.7)	NE (1.5, NE)	0.6093 (0.2551, 1.4554) 0.2648	0.2615	
Europe + Israel	166	56 (33.7)	110 (66.3)	23.6 (13.3, NE)	85	18 (21.2)	67 (78.8)	NE (11.1, NE)	1.2336 (0.7207, 2.1117) 0.4439	0.4443	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	200	74 (37.0)	126 (63.0)	16.9 (13.3, NE)	105	37 (35.2)	68 (64.8)	11.1 (4.2, NE)	0.6695 (0.4485, 0.9992) 0.0496	0.0503	0.0890
1	173	57 (32.9)	116 (67.1)	NE (16.6, NE)	79	21 (26.6)	58 (73.4)	NE (11.3, NE)	1.1908 (0.7198, 1.9698) 0.4966	0.5027	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.9719
0	60	23 (38.3)	37 (61.7)	NE (3.1, NE)	34	13 (38.2)	21 (61.8)	7.1 (1.7, NE)	0.8053 (0.4071, 1.5928) 0.5337	0.5339	
1	108	30 (27.8)	78 (72.2)	17.3 (16.6, NE)	51	14 (27.5)	37 (72.5)	11.3 (7.7, NE)	0.8674 (0.4591, 1.6385) 0.6611	0.6622	
2	115	42 (36.5)	73 (63.5)	14.9 (11.2, NE)	54	16 (29.6)	38 (70.4)	NE (4.4, NE)	0.8716 (0.4833, 1.5717) 0.6477	0.6453	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	36 (40.0)	54 (60.0)	16.3 (8.3, NE)	45	15 (33.3)	30 (66.7)	NE (3.1, NE)	0.8634 (0.4683, 1.5916) 0.6378	0.6344

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.5708
PD	174	59 (33.9)	115 (66.1)	16.3 (14.1, NE)	85	20 (23.5)	65 (76.5)	NE (NE, NE)	1.0807 (0.6477, 1.8031) 0.7664	0.7630	
PR	48	20 (41.7)	28 (58.3)	NE (6.2, NE)	22	8 (36.4)	14 (63.6)	4.3 (2.9, NE)	0.7167 (0.3118, 1.6474) 0.4328	0.4336	
SD	82	31 (37.8)	51 (62.2)	NE (8.2, NE)	55	21 (38.2)	34 (61.8)	11.1 (4.9, NE)	0.7929 (0.4511, 1.3936) 0.4199	0.4201	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.3247
Yes	37	11 (29.7)	26 (70.3)	NE (7.1, NE)	15	5 (33.3)	10 (66.7)	4.3 (0.8, NE)	0.4529 (0.1525, 1.3449) 0.1538	0.1425
No	336	120 (35.7)	216 (64.3)	17.3 (14.1, NE)	169	53 (31.4)	116 (68.6)	NE (11.1, NE)	0.8894 (0.6413, 1.2336) 0.4826	0.4822

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.5562
Yes	24	8 (33.3)	16 (66.7)	NE (7.1, NE)	8	3 (37.5)	5 (62.5)	NE (0.8, NE)	0.4854 (0.1248, 1.8875) 0.2969	0.2870
No	349	123 (35.2)	226 (64.8)	17.3 (14.9, NE)	176	55 (31.3)	121 (68.8)	NE (7.7, NE)	0.8741 (0.6337, 1.2058) 0.4123	0.4119

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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## Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.6115
Normal Function	202	66 (32.7)	136 (67.3)	23.6 (23.6, NE)	87	22 (25.3)	65 (74.7)	NE (NE, NE)	0.9912 (0.6089, 1.6136) 0.9716	0.9766	
Mild Impairment	123	46 (37.4)	77 (62.6)	16.3 (10.0, NE)	69	26 (37.7)	43 (62.3)	7.1 (2.9, NE)	0.7191 (0.4408, 1.1731) 0.1866	0.1842	
Moderate Impairment	41	17 (41.5)	24 (58.5)	13.3 (7.1, NE)	23	9 (39.1)	14 (60.9)	11.3 (5.9, NE)	1.0318 (0.4584, 2.3224) 0.9397	0.9456	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Hepatic function at baseline										0.4428
Normal Function	170	69 (40.6)	101 (59.4)	16.3 (10.8, NE)	98	32 (32.7)	66 (67.3)	NE (6.1, NE)	0.9584 (0.6269, 1.4652)	0.8409
Mild Impairment	195	60 (30.8)	135 (69.2)	NE (16.6, NE)	84	25 (29.8)	59 (70.2)	NE (11.3, NE)	0.7638 (0.4765, 1.2243)	0.2630

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.8983
Yes	332	115 (34.6)	217 (65.4)	17.3 (14.1, NE)	157	50 (31.8)	107 (68.2)	NE (11.1, NE)	0.8422 (0.6024, 1.1772) 0.3148	0.3154	
No	41	16 (39.0)	25 (61.0)	23.6 (3.0, 23.6)	27	8 (29.6)	19 (70.4)	5.9 (4.9, NE)	0.9942 (0.4199, 2.3541) 0.9894	0.9887	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.6247
Positive	331	116 (35.0)	215 (65.0)	17.3 (14.9, NE)	163	50 (30.7)	113 (69.3)	NE (11.1, NE)	0.8614 (0.6159, 1.2046) 0.3831	0.3829	
Negative	42	15 (35.7)	27 (64.3)	NE (2.8, NE)	21	8 (38.1)	13 (61.9)	5.9 (1.4, NE)	0.8125 (0.3438, 1.9199) 0.6359	0.6305	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Hormon receptor status (derived)										0.4497
Positive	333	117 (35.1)	216 (64.9)	17.3 (14.9, NE)	166	51 (30.7)	115 (69.3)	NE (11.1, NE)	0.8691 (0.6231, 1.2122)	0.4080
Negative	40	14 (35.0)	26 (65.0)	NE (2.9, NE)	18	7 (38.9)	11 (61.1)	5.9 (1.4, NE)	0.7088 (0.2853, 1.7609)	0.4540

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.3379
HER2 IHC 1+	214	86 (40.2)	128 (59.8)	15.3 (6.4, NE)	107	46 (43.0)	61 (57.0)	5.4 (2.7, NE)	0.7128 (0.4975, 1.0212) 0.0650	0.0642	
HER2 IHC 2+/ISH Negative	159	75 (47.2)	84 (52.8)	8.5 (5.6, NE)	77	33 (42.9)	44 (57.1)	6.1 (4.2, NE)	0.8889 (0.5887, 1.3420) 0.5751	0.5666	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.8741
1	221	103 (46.6)	118 (53.4)	7.8 (5.6, NE)	100	50 (50.0)	50 (50.0)	4.7 (2.8, 15.5)	0.7664 (0.5460, 1.0757)	0.1217	
>=2	151	57 (37.7)	94 (62.3)	NE (6.3, NE)	83	29 (34.9)	54 (65.1)	NE (4.2, NE)	0.8130 (0.5186, 1.2746)	0.3600	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.3841
Yes	235	105 (44.7)	130 (55.3)	7.2 (5.7, NE)	118	49 (41.5)	69 (58.5)	5.8 (4.2, NE)	0.8400 (0.5970, 1.1817) 0.3166	0.3073	
No	98	41 (41.8)	57 (58.2)	NE (5.6, NE)	48	23 (47.9)	25 (52.1)	5.9 (1.9, NE)	0.6537 (0.3913, 1.0919) 0.1043	0.1046	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1572
<65	290	124 (42.8)	166 (57.2)	15.3 (6.4, NE)	136	60 (44.1)	76 (55.9)	5.4 (2.8, NE)	0.7017 (0.5144, 0.9573) 0.0254	0.0238	
>=65	83	37 (44.6)	46 (55.4)	7.2 (4.2, NE)	48	19 (39.6)	29 (60.4)	9.5 (4.6, NE)	1.0962 (0.6296, 1.9083) 0.7455	0.7424	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0500
<75	359	151 (42.1)	208 (57.9)	15.3 (7.0, NE)	175	75 (42.9)	100 (57.1)	5.8 (4.2, NE)	0.7464 (0.5649, 0.9863) 0.0397	0.0381	
>=75	14	10 (71.4)	4 (28.6)	4.2 (1.6, 9.2)	9	4 (44.4)	5 (55.6)	15.8 (1.4, 15.8)	2.8994 (0.8901, 9.4452) 0.0773	0.0649	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.7580
White	176	81 (46.0)	95 (54.0)	7.0 (4.9, NE)	91	42 (46.2)	49 (53.8)	4.6 (2.8, 15.5)	0.7346 (0.5045, 1.0696) 0.1076	0.1043	
Non-White	197	80 (40.6)	117 (59.4)	NE (7.2, NE)	92	37 (40.2)	55 (59.8)	9.5 (4.4, NE)	0.8351 (0.5649, 1.2344) 0.3660	0.3621	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Region										0.5463
Asia	147	63 (42.9)	84 (57.1)	NE (6.3, NE)	66	27 (40.9)	39 (59.1)	NE (4.2, NE)	0.8792 (0.5598, 1.3807) 0.5761	0.5749
North America	60	21 (35.0)	39 (65.0)	9.5 (5.7, 22.3)	33	13 (39.4)	20 (60.6)	3.7 (1.2, NE)	0.5124 (0.2501, 1.0501) 0.0678	0.0625
Europe + Israel	166	77 (46.4)	89 (53.6)	7.2 (4.2, NE)	85	39 (45.9)	46 (54.1)	5.4 (3.9, 15.5)	0.8328 (0.5655, 1.2266) 0.3544	0.3453

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.0743
0	200	86 (43.0)	114 (57.0)	15.3 (7.0, NE)	105	49 (46.7)	56 (53.3)	5.4 (2.1, 15.5)	0.6263 (0.4398, 0.8919) 0.0095	0.0089	
1	173	75 (43.4)	98 (56.6)	9.5 (4.2, NE)	79	30 (38.0)	49 (62.0)	NE (4.2, NE)	1.0566 (0.6908, 1.6161) 0.7994	0.8029	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.9488
0	60	27 (45.0)	33 (55.0)	7.8 (3.0, NE)	34	15 (44.1)	19 (55.9)	4.2 (1.7, NE)	0.7655 (0.4054, 1.4453) 0.4099	0.4087
1	108	39 (36.1)	69 (63.9)	22.3 (6.2, NE)	51	21 (41.2)	30 (58.8)	9.5 (4.7, NE)	0.7740 (0.4538, 1.3200) 0.3469	0.3413
2	115	53 (46.1)	62 (53.9)	8.5 (4.4, NE)	54	25 (46.3)	29 (53.7)	4.6 (2.1, NE)	0.7336 (0.4543, 1.1845) 0.2051	0.2025

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	42 (46.7)	48 (53.3)	8.5 (4.9, NE)	45	18 (40.0)	27 (60.0)	5.8 (2.1, NE)	0.8884 (0.5091, 1.5502) 0.6770	0.6738

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.7541
PD	174	72 (41.4)	102 (58.6)	8.5 (5.6, NE)	85	36 (42.4)	49 (57.6)	4.6 (3.0, NE)	0.7357 (0.4925, 1.0990) 0.1339	0.1295
PR	48	20 (41.7)	28 (58.3)	NE (2.9, NE)	22	9 (40.9)	13 (59.1)	6.7 (0.9, NE)	0.7055 (0.3201, 1.5548) 0.3869	0.3898
SD	82	35 (42.7)	47 (57.3)	10.3 (6.1, NE)	55	22 (40.0)	33 (60.0)	15.5 (4.4, NE)	0.8935 (0.5230, 1.5263) 0.6802	0.6813

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Symptom Scales/Systemic Therapy Side Effects

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Reported history of CNS metastases										0.9514
Yes	37	14 (37.8)	23 (62.2)	22.3 (5.6, 22.3)	15	4 (26.7)	11 (73.3)	NE (0.8, NE)	0.7136 (0.2297, 2.2171)	0.5610
No	336	147 (43.8)	189 (56.3)	9.2 (6.2, NE)	169	75 (44.4)	94 (55.6)	5.9 (4.2, 15.8)	0.8041 (0.6082, 1.0631)	0.1235

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.2676
Yes	24	5 (20.8)	19 (79.2)	NE (6.1, NE)	8	3 (37.5)	5 (62.5)	NE (0.8, NE)	0.3474 (0.0813, 1.4847) 0.1537	0.1375	
No	349	156 (44.7)	193 (55.3)	8.5 (6.0, NE)	176	76 (43.2)	100 (56.8)	5.9 (4.2, 15.8)	0.8206 (0.6229, 1.0810) 0.1596	0.1566	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.8783
Normal Function	202	90 (44.6)	112 (55.4)	8.5 (5.7, NE)	87	38 (43.7)	49 (56.3)	4.2 (2.8, NE)	0.7498 (0.5116, 1.0988) 0.1397	0.1338	
Mild Impairment	123	53 (43.1)	70 (56.9)	10.3 (5.6, NE)	69	27 (39.1)	42 (60.9)	6.1 (2.8, NE)	0.8723 (0.5473, 1.3904) 0.5658	0.5660	
Moderate Impairment	41	17 (41.5)	24 (58.5)	NE (4.2, NE)	23	11 (47.8)	12 (52.2)	9.5 (4.2, NE)	0.8895 (0.4162, 1.9009) 0.7625	0.7592	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Hepatic function at baseline										0.3279
Normal Function	170	86 (50.6)	84 (49.4)	7.0 (4.2, NE)	98	44 (44.9)	54 (55.1)	5.9 (3.1, NE)	0.9359 (0.6498, 1.3480)	0.7171
Mild Impairment	195	74 (37.9)	121 (62.1)	NE (7.2, NE)	84	33 (39.3)	51 (60.7)	5.4 (4.2, NE)	0.7015 (0.4638, 1.0610)	0.0885

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.7406
Yes	332	145 (43.7)	187 (56.3)	9.5 (6.2, NE)	157	67 (42.7)	90 (57.3)	5.9 (4.2, 15.8)	0.7952 (0.5946, 1.0636) 0.1225	0.1211	
No	41	16 (39.0)	25 (61.0)	NE (4.4, NE)	27	12 (44.4)	15 (55.6)	5.9 (3.0, NE)	0.6957 (0.3266, 1.4820) 0.3471	0.3416	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Hormon receptor status (IXRS)										0.5216
Positive	331	145 (43.8)	186 (56.2)	10.5 (6.2, NE)	163	68 (41.7)	95 (58.3)	6.1 (4.2, 15.8)	0.8170 (0.6117, 1.0913)	0.1683
Negative	42	16 (38.1)	26 (61.9)	9.2 (4.2, NE)	21	11 (52.4)	10 (47.6)	4.2 (1.7, NE)	0.6236 (0.2877, 1.3517)	0.2268

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Hormon receptor status (derived)										0.8040
Positive	333	145 (43.5)	188 (56.5)	10.5 (6.4, NE)	166	72 (43.4)	94 (56.6)	5.9 (4.2, 15.8)	0.7796 (0.5868, 1.0357) 0.0858	0.0836
Negative	40	16 (40.0)	24 (60.0)	8.5 (2.9, NE)	18	7 (38.9)	11 (61.1)	5.9 (1.5, NE)	0.9089 (0.3727, 2.2161) 0.8336	0.8328

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.6677
HER2 IHC 1+	214	60 (28.0)	154 (72.0)	NE (20.3, NE)	107	22 (20.6)	85 (79.4)	NE (NE, NE)	1.0340 (0.6312, 1.6938) 0.8943	0.8933	
HER2 IHC 2+/ISH Negative	159	37 (23.3)	122 (76.7)	NE (17.1, NE)	77	15 (19.5)	62 (80.5)	NE (NE, NE)	0.7611 (0.4137, 1.4004) 0.3802	0.3781	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.1000
1	221	62 (28.1)	159 (71.9)	NE (20.3, NE)	100	18 (18.0)	82 (82.0)	NE (NE, NE)	1.2410 (0.7322, 2.1033) 0.4226	0.4211
>=2	151	35 (23.2)	116 (76.8)	NE (17.1, NE)	83	19 (22.9)	64 (77.1)	NE (8.1, NE)	0.5945 (0.3338, 1.0591) 0.0776	0.0747

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.1960
Yes	235	64 (27.2)	171 (72.8)	NE (NE, NE)	118	22 (18.6)	96 (81.4)	NE (NE, NE)	1.0848 (0.6653, 1.7690) 0.7441	0.7458	
No	98	23 (23.5)	75 (76.5)	NE (20.3, NE)	48	12 (25.0)	36 (75.0)	NE (8.1, NE)	0.5899 (0.2884, 1.2068) 0.1484	0.1441	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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[c] Two-sided p-value from unstratified log-rank test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0047
<65	290	72 (24.8)	218 (75.2)	NE (NE, NE)	136	32 (23.5)	104 (76.5)	NE (NE, NE)	0.6572 (0.4305, 1.0031) 0.0517	0.0502	
>=65	83	25 (30.1)	58 (69.9)	20.3 (10.2, 20.3)	48	5 (10.4)	43 (89.6)	NE (NE, NE)	2.6889 (1.0200, 7.0886) 0.0455	0.0374	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Age										0.6652
<75	359	95 (26.5)	264 (73.5)	NE (20.3, NE)	175	36 (20.6)	139 (79.4)	NE (NE, NE)	0.8687 (0.5885, 1.2824) 0.4788	0.4776
>=75	14	2 (14.3)	12 (85.7)	NE (1.6, NE)	9	1 (11.1)	8 (88.9)	NE (1.4, NE)	1.5289 (0.1385, 16.8724) 0.7289	0.7269

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.6643
White	176	41 (23.3)	135 (76.7)	NE (NE, NE)	91	17 (18.7)	74 (81.3)	NE (NE, NE)	0.8212 (0.4626, 1.4576) 0.5009	0.4991	
Non-White	197	56 (28.4)	141 (71.6)	NE (17.1, NE)	92	20 (21.7)	72 (78.3)	NE (NE, NE)	0.9814 (0.5855, 1.6449) 0.9432	0.9416	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.7677
Asia	147	43 (29.3)	104 (70.7)	NE (17.1, NE)	66	16 (24.2)	50 (75.8)	NE (8.5, NE)	0.8732 (0.4884, 1.5612) 0.6475	0.6453	
North America	60	14 (23.3)	46 (76.7)	NE (7.8, NE)	33	4 (12.1)	29 (87.9)	NE (NE, NE)	1.3579 (0.4414, 4.1780) 0.5936	0.5907	
Europe + Israel	166	40 (24.1)	126 (75.9)	NE (NE, NE)	85	17 (20.0)	68 (80.0)	NE (NE, NE)	0.8358 (0.4699, 1.4867) 0.5416	0.5391	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.6554
0	200	52 (26.0)	148 (74.0)	NE (20.3, NE)	105	21 (20.0)	84 (80.0)	NE (NE, NE)	0.8422 (0.5042, 1.4066) 0.5116	0.5121	
1	173	45 (26.0)	128 (74.0)	NE (14.7, NE)	79	16 (20.3)	63 (79.7)	NE (8.5, NE)	1.0080 (0.5650, 1.7984) 0.9785	0.9818	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.2834
0	60	17 (28.3)	43 (71.7)	NE (9.3, NE)	34	7 (20.6)	27 (79.4)	NE (5.8, NE)	0.9216 (0.3796, 2.2375)	0.8601
1	108	25 (23.1)	83 (76.9)	NE (NE, NE)	51	8 (15.7)	43 (84.3)	NE (NE, NE)	1.3198 (0.5938, 2.9337)	0.4954
2	115	30 (26.1)	85 (73.9)	NE (NE, NE)	54	15 (27.8)	39 (72.2)	NE (4.2, NE)	0.5662 (0.2978, 1.0764)	0.0785

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	25 (27.8)	65 (72.2)	17.1 (14.7, NE)	45	7 (15.6)	38 (84.4)	NE (NE, NE)	1.1213 (0.4764, 2.6391) 0.7932	0.7935	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.3278
PD	174	41 (23.6)	133 (76.4)	NE (16.3, NE)	85	16 (18.8)	69 (81.2)	NE (NE, NE)	0.7828 (0.4326, 1.4164) 0.4183	0.4168	
PR	48	13 (27.1)	35 (72.9)	NE (14.7, NE)	22	6 (27.3)	16 (72.7)	NE (3.0, NE)	0.6308 (0.2335, 1.7041) 0.3635	0.3569	
SD	82	21 (25.6)	61 (74.4)	NE (20.3, NE)	55	8 (14.5)	47 (85.5)	NE (NE, NE)	1.4707 (0.6475, 3.3403) 0.3567	0.3543	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.2077
Yes	37	11 (29.7)	26 (70.3)	NE (8.3, NE)	15	1 (6.7)	14 (93.3)	NE (3.0, NE)	2.1113 (0.2636, 16.9086) 0.4814	0.4716
No	336	86 (25.6)	250 (74.4)	NE (20.3, NE)	169	36 (21.3)	133 (78.7)	NE (NE, NE)	0.8583 (0.5785, 1.2735) 0.4478	0.4468

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.7945
Yes	24	5 (20.8)	19 (79.2)	NE (9.3, NE)	8	1 (12.5)	7 (87.5)	NE (3.0, NE)	0.7218 (0.0780, 6.6828)	0.7734 0.7740
No	349	92 (26.4)	257 (73.6)	NE (20.3, NE)	176	36 (20.5)	140 (79.5)	NE (NE, NE)	0.9167 (0.6204, 1.3545)	0.6613 0.6623

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline									0.0053
Normal Function	202	50 (24.8)	152 (75.2) (20.3, NE)	87	19 (21.8)	68 (78.2) (NE, NE)	0.6860 (0.4012, 1.1728) 0.1684	0.1664	
Mild Impairment	123	33 (26.8)	90 (73.2) (16.3, NE)	69	16 (23.2)	53 (76.8) (7.1, NE)	0.7458 (0.4036, 1.3780) 0.3491	0.3473	
Moderate Impairment	41	13 (31.7)	28 (68.3) (11.8, NE)	23	1 (4.3)	22 (95.7) (NE, NE)	8.5583 (1.1161, 65.6263) 0.0389	0.0131	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.4642
Normal Function	170	53 (31.2)	117 (68.8)	NE (17.1, NE)	98	21 (21.4)	77 (78.6)	NE (NE, NE)	1.0847 (0.6508, 1.8080) 0.7551	0.7567	
Mild Impairment	195	43 (22.1)	152 (77.9)	NE (NE, NE)	84	15 (17.9)	69 (82.1)	NE (NE, NE)	0.7846 (0.4312, 1.4280) 0.4273	0.4266	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1584
Yes	332	84 (25.3)	248 (74.7)	NE (20.3, NE)	157	28 (17.8)	129 (82.2)	NE (NE, NE)	1.0314 (0.6694, 1.5890) 0.8887	0.8887	
No	41	13 (31.7)	28 (68.3)	NE (10.2, NE)	27	9 (33.3)	18 (66.7)	NE (3.1, NE)	0.5257 (0.2160, 1.2792) 0.1564	0.1488	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.9929
Positive	331	87 (26.3)	244 (73.7)	NE (20.3, NE)	163	33 (20.2)	130 (79.8)	NE (NE, NE)	0.9288 (0.6194, 1.3929)	0.7199	
Negative	42	10 (23.8)	32 (76.2)	17.1 (9.3, NE)	21	4 (19.0)	17 (81.0)	NE (5.8, NE)	0.6956 (0.2036, 2.3768)	0.5607	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.6520
Positive	333	86 (25.8)	247 (74.2)	NE (20.3, NE)	166	34 (20.5)	132 (79.5)	NE (NE, NE)	0.9009 (0.6027, 1.3464) 0.6106	0.6091	
Negative	40	11 (27.5)	29 (72.5)	17.1 (9.3, NE)	18	3 (16.7)	15 (83.3)	NE (5.8, NE)	0.9487 (0.2515, 3.5779) 0.9380	0.9380	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.3999
HER2 IHC 1+	214	61 (28.5)	153 (71.5)	NE (13.4, NE)	107	27 (25.2)	80 (74.8)	NE (6.3, NE)	0.7138 (0.4506, 1.1307)	0.1509	0.1494
HER2 IHC 2+/ISH Negative	159	41 (25.8)	118 (74.2)	NE (NE, NE)	77	24 (31.2)	53 (68.8)	12.3 (5.8, NE)	0.5224 (0.3116, 0.8758)	0.0138	0.0124

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.1748
1	221	67 (30.3)	154 (69.7)	NE (15.8, NE)	100	28 (28.0)	72 (72.0)	NE (6.3, NE)	0.8071 (0.5174, 1.2591) 0.3450	0.3446
>=2	151	35 (23.2)	116 (76.8)	NE (NE, NE)	83	23 (27.7)	60 (72.3)	12.3 (5.4, NE)	0.3932 (0.2269, 0.6816) 0.0009	0.0006

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.5674
Yes	235	61 (26.0)	174 (74.0)	NE (NE, NE)	118	27 (22.9)	91 (77.1)	NE (NE, NE)	0.6947 (0.4371, 1.1040) 0.1233	0.1217	
No	98	32 (32.7)	66 (67.3)	NE (13.4, NE)	48	19 (39.6)	29 (60.4)	7.0 (4.7, NE)	0.5423 (0.3055, 0.9625) 0.0366	0.0339	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8217
<65	290	84 (29.0)	206 (71.0)	NE (15.8, NE)	136	38 (27.9)	98 (72.1)	12.3 (5.8, NE)	0.6245 (0.4224, 0.9233) 0.0183	0.0173	
>=65	83	18 (21.7)	65 (78.3)	NE (NE, NE)	48	13 (27.1)	35 (72.9)	NE (7.0, NE)	0.5695 (0.2751, 1.1787) 0.1293	0.1265	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9185
<75	359	100 (27.9)	259 (72.1)	NE (NE, NE)	175	49 (28.0)	126 (72.0)	12.3 (6.3, NE)	0.6084 (0.4291, 0.8628) 0.0053	0.0049	
>=75	14	2 (14.3)	12 (85.7)	NE (5.8, NE)	9	2 (22.2)	7 (77.8)	NE (1.4, NE)	0.6391 (0.0897, 4.5515) 0.6549	0.6522	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.5857
White	176	48 (27.3)	128 (72.7)	NE (12.7, NE)	91	26 (28.6)	65 (71.4)	12.3 (5.4, NE)	0.5341 (0.3272, 0.8720) 0.0122	0.0110	
Non-White	197	54 (27.4)	143 (72.6)	NE (NE, NE)	92	25 (27.2)	67 (72.8)	NE (6.1, NE)	0.7037 (0.4349, 1.1387) 0.1524	0.1504	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.9182
Asia	147	47 (32.0)	100 (68.0)	NE (NE, NE)	66	22 (33.3)	44 (66.7)	NE (5.4, NE)	0.6546 (0.3917, 1.0939) 0.1058	0.1036	
North America	60	14 (23.3)	46 (76.7)	NE (10.4, NE)	33	6 (18.2)	27 (81.8)	NE (4.5, NE)	0.6766 (0.2514, 1.8207) 0.4392	0.4368	
Europe + Israel	166	41 (24.7)	125 (75.3)	NE (NE, NE)	85	23 (27.1)	62 (72.9)	12.3 (6.3, NE)	0.5776 (0.3431, 0.9724) 0.0389	0.0367	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	200	60 (30.0)	140 (70.0)	NE (15.8, NE)	105	33 (31.4)	72 (68.6)	12.3 (5.1, NE)	0.4757 (0.3071, 0.7369) 0.0009	0.0007	0.1556
1	173	42 (24.3)	131 (75.7)	NE (NE, NE)	79	18 (22.8)	61 (77.2)	NE (7.0, NE)	0.8934 (0.5122, 1.5584) 0.6913	0.6905	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.8460
0	60	20 (33.3)	40 (66.7)	11.8 (7.7, NE)	34	10 (29.4)	24 (70.6)	7.0 (4.7, NE)	0.6930 (0.3194, 1.5040)	0.3463
1	108	25 (23.1)	83 (76.9)	NE (15.8, NE)	51	17 (33.3)	34 (66.7)	12.3 (5.7, NE)	0.5031 (0.2700, 0.9375)	0.0276
2	115	33 (28.7)	82 (71.3)	NE (NE, NE)	54	14 (25.9)	40 (74.1)	NE (5.1, NE)	0.6815 (0.3601, 1.2897)	0.2354

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	24 (26.7)	66 (73.3)	NE (13.4, NE)	45	10 (22.2)	35 (77.8)	NE (NE, NE)	0.6658 (0.3107, 1.4267) 0.2956	0.2934

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.3570
PD	174	44 (25.3)	130 (74.7)	NE (15.8, NE)	85	21 (24.7)	64 (75.3)	NE (5.8, NE)	0.6771 (0.3985, 1.1503) 0.1492	0.1473	
PR	48	10 (20.8)	38 (79.2)	NE (NE, NE)	22	7 (31.8)	15 (68.2)	NE (2.7, NE)	0.3204 (0.1175, 0.8736) 0.0261	0.0197	
SD	82	27 (32.9)	55 (67.1)	NE (10.6, NE)	55	16 (29.1)	39 (70.9)	NE (5.7, NE)	0.7577 (0.4032, 1.4237) 0.3886	0.3869	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]	
Reported history of CNS metastases										0.2699	
Yes	37	8 (21.6)	29 (78.4)	NE (NE, NE)	15	1 (6.7)	14 (93.3)	NE (1.6, NE)	2.0444 (0.2526, 16.5446)	0.4895	
No	336	94 (28.0)	242 (72.0)	NE (NE, NE)	169	50 (29.6)	119 (70.4)	12.3 (6.3, NE)	0.5997 (0.4226, 0.8511)	0.0039	

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 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.6013
Yes	24	5 (20.8)	19 (79.2)	NE (11.1, NE)	8	1 (12.5)	7 (87.5)	NE (1.6, NE)	1.0957 (0.1231, 9.7545) 0.9347	0.9251
No	349	97 (27.8)	252 (72.2)	NE (NE, NE)	176	50 (28.4)	126 (71.6)	12.3 (6.3, NE)	0.6141 (0.4336, 0.8698) 0.0060	0.0057

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Renal function at baseline										0.1969
Normal Function	202	51 (25.2)	151 (74.8)	NE (NE, NE)	87	25 (28.7)	62 (71.3)	NE (5.4, NE)	0.5099 (0.3117, 0.8341) 0.0073	0.0063
Mild Impairment	123	36 (29.3)	87 (70.7)	NE (13.4, NE)	69	20 (29.0)	49 (71.0)	NE (5.7, NE)	0.5866 (0.3351, 1.0269) 0.0619	0.0608
Moderate Impairment	41	13 (31.7)	28 (68.3)	NE (9.1, NE)	23	5 (21.7)	18 (78.3)	NE (12.3, NE)	1.3651 (0.4843, 3.8478) 0.5561	0.5545

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.5186
Normal Function	170	56 (32.9)	114 (67.1)	NE (15.8, NE)	98	30 (30.6)	68 (69.4)	12.3 (6.1, NE)	0.7100 (0.4523, 1.1145)	0.1350	
Mild Impairment	195	45 (23.1)	150 (76.9)	NE (NE, NE)	84	20 (23.8)	64 (76.2)	NE (NE, NE)	0.5703 (0.3325, 0.9783)	0.0395	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline visceral disease										0.9067
Yes	332	87 (26.2)	245 (73.8)	NE (NE, NE)	157	42 (26.8)	115 (73.2)	NE (12.3, NE)	0.6145 (0.4225, 0.8939) 0.0109	0.0104
No	41	15 (36.6)	26 (63.4)	NE (5.1, NE)	27	9 (33.3)	18 (66.7)	5.9 (3.9, NE)	0.7409 (0.3180, 1.7263) 0.4871	0.4879

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.8471
Positive	331	92 (27.8)	239 (72.2)	NE (NE, NE)	163	45 (27.6)	118 (72.4)	NE (7.0, NE)	0.6239 (0.4339, 0.8970) 0.0109	0.0103	
Negative	42	10 (23.8)	32 (76.2)	NE (11.8, NE)	21	6 (28.6)	15 (71.4)	NE (2.3, NE)	0.6198 (0.2189, 1.7547) 0.3676	0.3573	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.9379
Positive	333	92 (27.6)	241 (72.4)	NE (NE, NE)	166	46 (27.7)	120 (72.3)	NE (6.3, NE)	0.6187 (0.4313, 0.8875) 0.0091	0.0086	
Negative	40	10 (25.0)	30 (75.0)	NE (11.8, NE)	18	5 (27.8)	13 (72.2)	NE (1.5, NE)	0.6404 (0.2134, 1.9221) 0.4268	0.4197	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.8248
HER2 IHC 1+	214	23 (10.7)	191 (89.3)	7.2 (1.6, NE)	107	8 (7.5)	99 (92.5)	NE (0.8, NE)	0.9382 (0.4174, 2.1087)	0.8786	
HER2 IHC 2+/ISH Negative	159	19 (11.9)	140 (88.1)	9.7 (2.9, NE)	77	8 (10.4)	69 (89.6)	NE (1.0, NE)	0.7753 (0.3338, 1.8006)	0.5569	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.9367
1	221	30 (13.6)	191 (86.4)	5.6 (1.6, 9.9)	100	12 (12.0)	88 (88.0)	2.1 (1.0, NE)	0.8794 (0.4455, 1.7359)	0.7139
>=2	151	12 (7.9)	139 (92.1)	NE (7.4, NE)	83	4 (4.8)	79 (95.2)	NE (0.7, NE)	0.8699 (0.2788, 2.7144)	0.8058

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.3854
Yes	235	25 (10.6)	210 (89.4)	9.9 (2.9, NE)	118	8 (6.8)	110 (93.2)	NE (1.2, NE)	0.9499 (0.4219, 2.1385) 0.9012	0.9042	
No	98	13 (13.3)	85 (86.7)	4.3 (1.3, NE)	48	7 (14.6)	41 (85.4)	1.5 (0.7, NE)	0.6398 (0.2532, 1.6166) 0.3450	0.3322	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Age										0.8282
<65	290	34 (11.7)	256 (88.3)	7.4 (2.9, NE)	136	10 (7.4)	126 (92.6)	NE (1.0, NE)	0.8764 (0.4301, 1.7860)	0.7105
>=65	83	8 (9.6)	75 (90.4)	6.7 (0.9, NE)	48	6 (12.5)	42 (87.5)	2.8 (0.7, NE)	0.8927 (0.3069, 2.5965)	0.8407

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0530
<75	359	40 (11.1)	319 (88.9)	9.7 (3.0, NE)	175	16 (9.1)	159 (90.9)	NE (1.2, NE)	0.7847 (0.4359, 1.4125) 0.4188	0.4189	
>=75	14	2 (14.3)	12 (85.7)	1.2 (0.9, 1.6)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9991	0.2253	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.6857
White	176	17 (9.7)	159 (90.3)	12.9 (1.6, NE)	91	8 (8.8)	83 (91.2)	NE (0.8, NE)	0.8165 (0.3478, 1.9169)	0.6505	
Non-White	197	25 (12.7)	172 (87.3)	7.4 (2.7, NE)	92	8 (8.7)	84 (91.3)	NE (1.0, NE)	0.9312 (0.4168, 2.0804)	0.8621	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.3078
Asia	147	18 (12.2)	129 (87.8)	5.7 (1.4, NE)	66	8 (12.1)	58 (87.9)	2.1 (0.7, NE)	0.8143 (0.3490, 1.8999)	0.6312	
North America	60	2 (3.3)	58 (96.7)	NE (4.2, NE)	33	2 (6.1)	31 (93.9)	NE (1.0, NE)	0.2739 (0.0367, 2.0440)	0.1786	
Europe + Israel	166	22 (13.3)	144 (86.7)	7.2 (1.6, NE)	85	6 (7.1)	79 (92.9)	NE (0.8, NE)	1.2657 (0.5111, 3.1343)	0.5899	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
ECOG PS										0.4030
0	200	19 (9.5)	181 (90.5)	5.6 (1.4, NE)	105	10 (9.5)	95 (90.5)	2.1 (1.0, NE)	0.7040 (0.3217, 1.5409)	0.3759
1	173	23 (13.3)	150 (86.7)	7.4 (2.9, NE)	79	6 (7.6)	73 (92.4)	NE (0.8, NE)	1.1571 (0.4695, 2.8517)	0.7436

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.4582
0	60	5 (8.3)	55 (91.7)	7.4 (0.7, NE)	34	2 (5.9)	32 (94.1)	NE (0.7, NE)	0.7311 (0.1390, 3.8465)	0.7710
1	108	17 (15.7)	91 (84.3)	2.9 (1.4, NE)	51	6 (11.8)	45 (88.2)	1.3 (0.7, NE)	0.7718 (0.3033, 1.9643)	0.6052
2	115	11 (9.6)	104 (90.4)	NE (2.9, NE)	54	6 (11.1)	48 (88.9)	2.1 (0.7, NE)	0.5714 (0.2062, 1.5830)	0.2748

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	9 (10.0)	81 (90.0)	9.9 (1.3, NE)	45	2 (4.4)	43 (95.6)	NE (1.2, NE)	1.7359 (0.3543, 8.5051) 0.4964	0.4950

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.0570
PD	174	20 (11.5)	154 (88.5)	9.7 (1.6, NE)	85	5 (5.9)	80 (94.1)	NE (1.2, NE)	1.2751 (0.4744, 3.4273)	0.6262
PR	48	6 (12.5)	42 (87.5)	5.7 (0.7, NE)	22	0	22 (100)	NE (NE, NE)	0.9969	0.1359
SD	82	8 (9.8)	74 (90.2)	6.7 (0.8, NE)	55	9 (16.4)	46 (83.6)	1.1 (0.7, NE)	0.6497 (0.2473, 1.7073)	0.3763

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.0215
Yes	37	3 (8.1)	34 (91.9)	NE (3.0, NE)	15	2 (13.3)	13 (86.7)	1.8 (0.7, 2.8)	0.0531 (0.0047, 0.5999)	0.0011	
No	336	39 (11.6)	297 (88.4)	6.7 (2.7, 12.5)	169	14 (8.3)	155 (91.7)	NE (1.2, NE)	1.1075 (0.5987, 2.0485)	0.7451	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.0193
Yes	24	3 (12.5)	21 (87.5)	NE (1.4, NE)	8	1 (12.5)	7 (87.5)	0.7 (NE, NE)	0.0000 (0.0000, ) 0.9966	0.0027
No	349	39 (11.2)	310 (88.8)	6.7 (2.8, 12.9)	176	15 (8.5)	161 (91.5)	NE (1.2, NE)	1.0086 (0.5535, 1.8380) 0.9777	0.9782

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 15SEP2022 – 12:16; Program name: T3\_EQ5D\_FD\_2\_FAS.sas; Output name: T3\_EORTCBR45\_FD\_2\_FAS.rtf

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## Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.8789
Normal Function	202	23 (11.4)	179 (88.6)	7.4 (2.9, NE)	87	6 (6.9)	81 (93.1)	NE (1.0, NE)	0.8406 (0.3370, 2.0971) 0.7097	0.6972	
Mild Impairment	123	14 (11.4)	109 (88.6)	9.7 (1.6, NE)	69	8 (11.6)	61 (88.4)	NE (0.8, NE)	0.9714 (0.4048, 2.3314) 0.9483	0.9620	
Moderate Impairment	41	5 (12.2)	36 (87.8)	5.7 (0.7, NE)	23	2 (8.7)	21 (91.3)	1.5 (0.7, NE)	0.6831 (0.1314, 3.5506) 0.6504	0.6485	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.9356
Normal Function	170	20 (11.8)	150 (88.2)	5.7 (1.6, NE)	98	9 (9.2)	89 (90.8)	NE (0.8, NE)	0.8826 (0.3955, 1.9696)	0.7572
Mild Impairment	195	22 (11.3)	173 (88.7)	7.4 (2.9, NE)	84	7 (8.3)	77 (91.7)	NE (1.0, NE)	0.8726 (0.3693, 2.0621)	0.7612

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.5314
Yes	332	33 (9.9)	299 (90.1)	9.9 (4.2, NE)	157	14 (8.9)	143 (91.1)	NE (1.2, NE)	0.7874 (0.4185, 1.4812) 0.4584	0.4633	
No	41	9 (22.0)	32 (78.0)	2.1 (0.7, 5.7)	27	2 (7.4)	25 (92.6)	NE (0.7, NE)	1.3520 (0.2915, 6.2703) 0.7000	0.7116	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Hormon receptor status (IXRS)										0.8298
Positive	331	39 (11.8)	292 (88.2)	7.2 (2.9, NE)	163	15 (9.2)	148 (90.8)	NE (1.2, NE)	0.8474 (0.4639, 1.5478)	0.5885
Negative	42	3 (7.1)	39 (92.9)	7.4 (0.7, NE)	21	1 (4.8)	20 (95.2)	NE (0.7, NE)	1.1588 (0.1194, 11.2510)	0.8767

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Hormon receptor status (derived)										0.6528
Positive	333	38 (11.4)	295 (88.6)	9.7 (2.9, NE)	166	15 (9.0)	151 (91.0)	NE (1.2, NE)	0.8349 (0.4559, 1.5290)	0.5575
Negative	40	4 (10.0)	36 (90.0)	7.4 (1.4, NE)	18	1 (5.6)	17 (94.4)	NE (0.7, NE)	1.5466 (0.1717, 13.9280)	0.6951

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

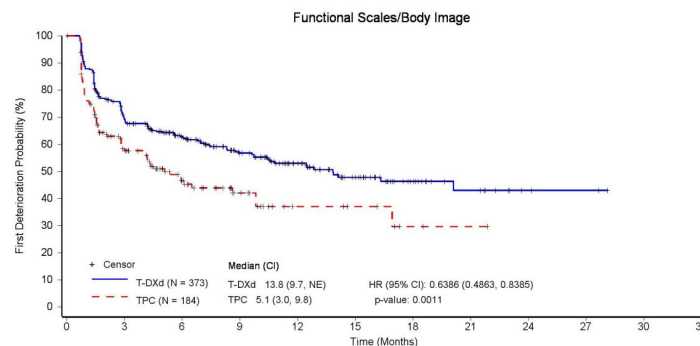
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.F.3.9.3 - EORTC QLQ-BR45 - First deterioration - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	222	162	115	75	44	23	13	3	2	0	0
TPC (N = 184)	184	76	39	20	8	6	2	1	0	0	0	0

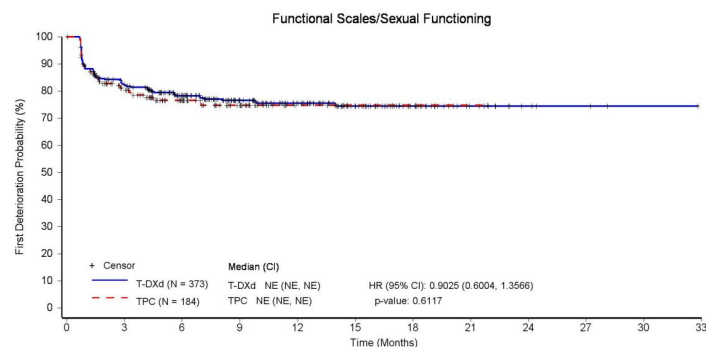
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	258	200	150	103	63	36	15	5	3	1	0
TPC (N = 184)	184	97	54	29	9	5	2	1	0	0	0	0

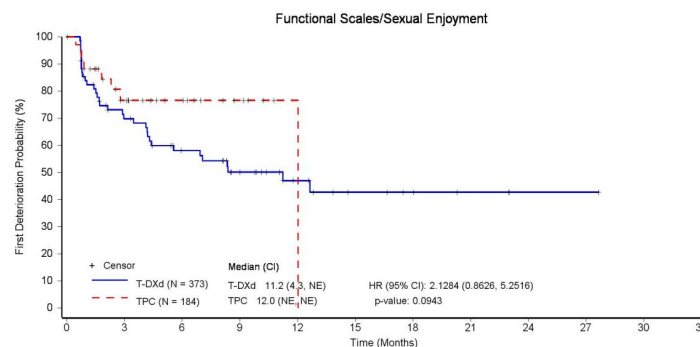
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

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DE.F.3.9.3 - EORTC QLQ-BR45 - First deterioration - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	43	31	22	12	7	5	3	1	1	0	0
TPC (N = 184)	184	18	11	5	1	0	0	0	0	0	0	0

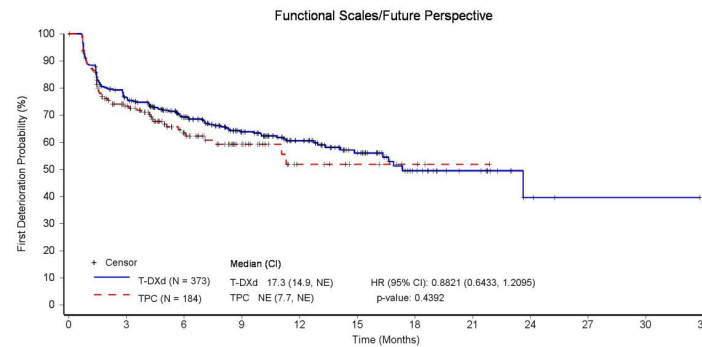
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	251	188	134	88	52	25	15	3	1	1	0
TPC (N = 184)	184	99	54	26	10	6	3	1	0	0	0	0

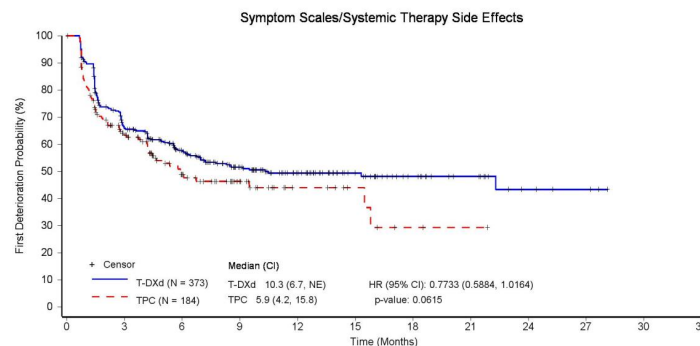
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	213	152	105	69	40	25	15	5	3	0	0
TPC (N = 184)	184	85	44	25	10	6	2	1	0	0	0	0

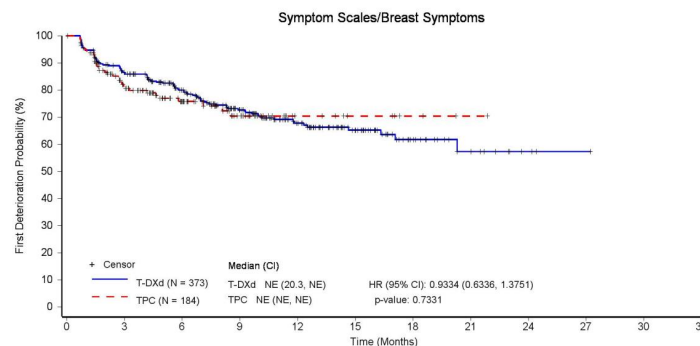
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	274	212	156	97	56	26	12	3	1	0	0
TPC (N = 184)	184	106	58	30	10	6	3	1	0	0	0	0

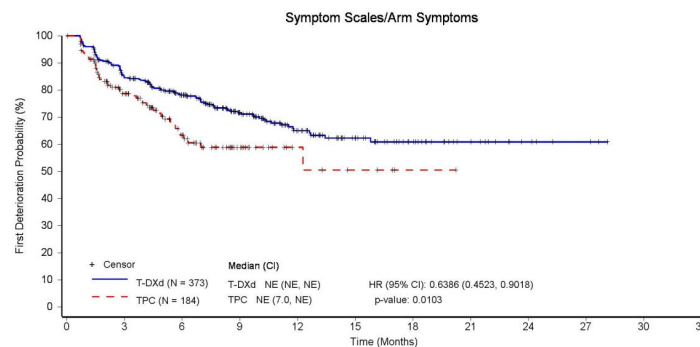
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	273	212	149	84	50	31	17	6	3	0	0
TPC (N = 184)	184	99	50	21	7	4	1	0	0	0	0	0

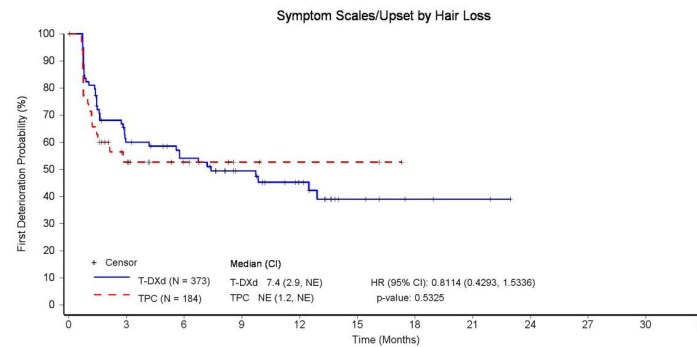
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	44	36	24	16	6	3	2	0	0	0	0
TPC (N = 184)	184	14	6	3	2	2	0	0	0	0	0	0

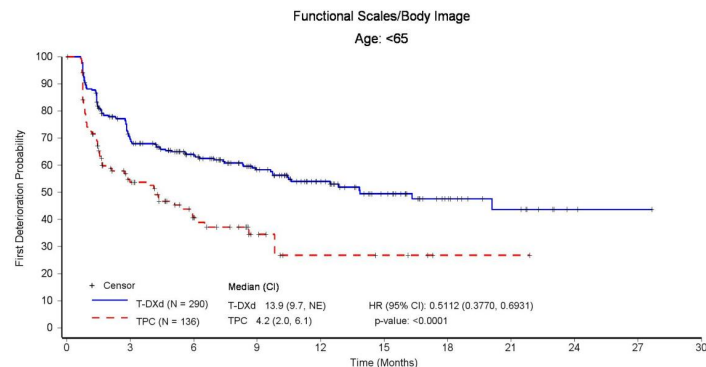
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:19; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F3\_EORTCQR45\_FD\_3\_FAS.rtf

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 Data Intelligence – Evidence Generation  
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DE.F.3.9.4 - EORTC QLQ-BR45 - First deterioration - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

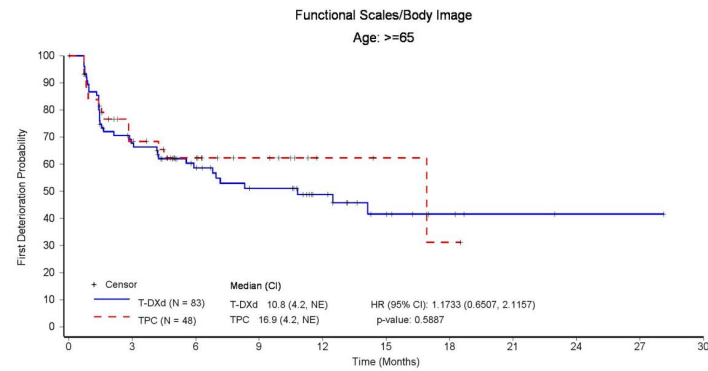
T-DXd (N = 290)	290	174	128	89	58	35	19	11	2	1	0
TPC (N = 136)	136	51	24	11	5	4	1	1	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:19; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCQR45\_FD\_4\_FAS.rtf

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Patients still at risk:

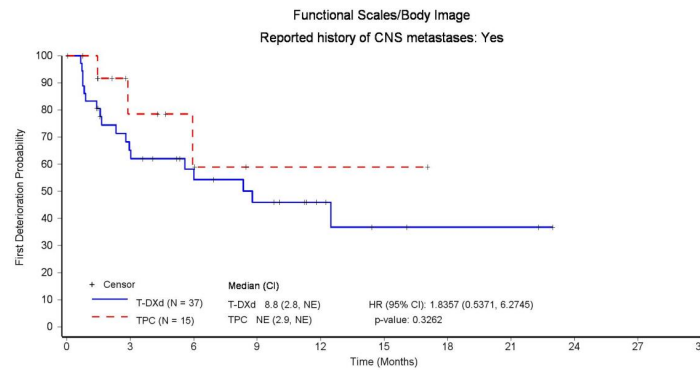
T-DXd (N = 83)	83	48	34	26	17	9	4	2	1	1	0
TPC (N = 48)	48	25	15	9	3	2	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:19; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCQR45\_FD\_4\_FAS.rtf

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Patients still at risk:

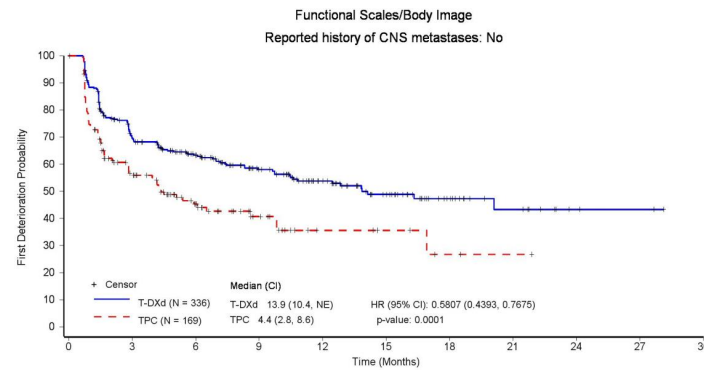
T-DXd (N = 37)	37	21	15	11	6	3	2	2	0	0	0
TPC (N = 15)	15	6	3	1	1	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:19; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCQR45\_FD\_4\_FAS.rtf

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Patients still at risk:

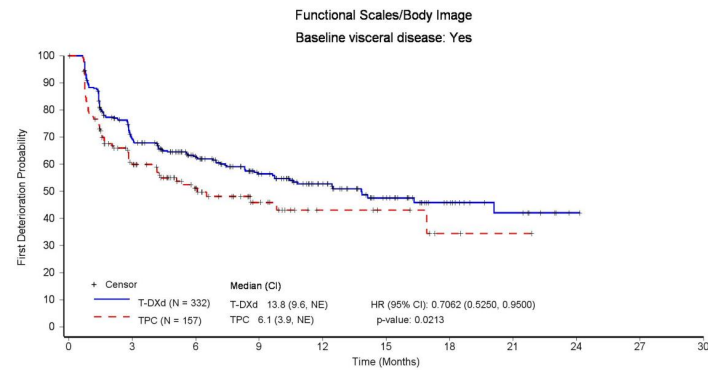
	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 336)	336	201	147	104	69	41	21	11	3	2	0
TPC (N = 169)	169	70	36	19	7	5	2	1	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:19; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCQR45\_FD\_4\_FAS.rtf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 332)	332	197	143	100	63	37	19	11	1	0	0
TPC (N = 157)	157	68	37	19	8	6	2	1	0	0	0

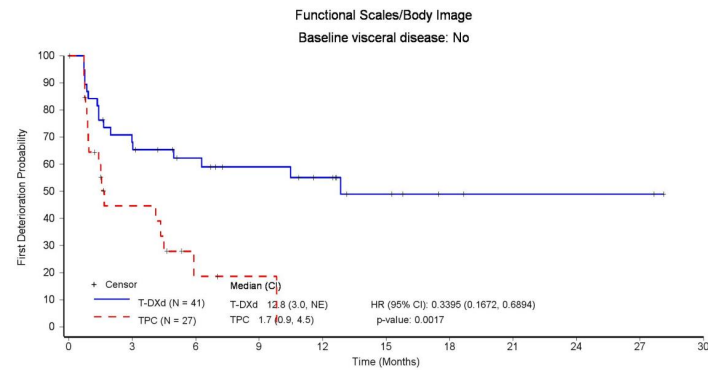
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:19; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCQR45\_FD\_4\_FAS.rtf

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 Data Intelligence – Evidence Generation  
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DE.F.3.9.4 - EORTC QLQ-BR45 - First deterioration - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

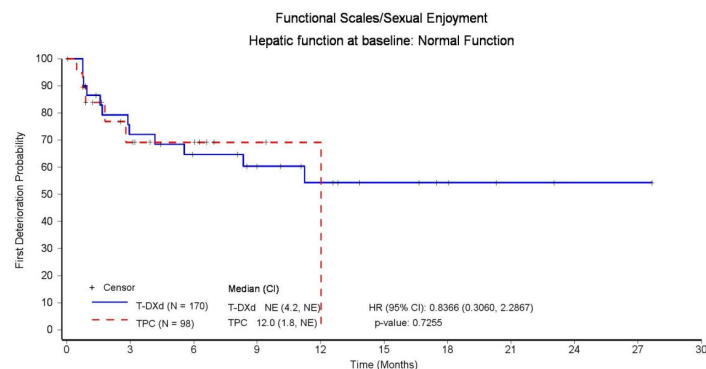
	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 41)	41	25	19	15	12	7	4	2	2	2	0
TPC (N = 27)	27	8	2	1	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:19; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCQR45\_FD\_4\_FAS.rtf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 170)	170	20	16	13	9	6	4	2	1	1	0
TPC (N = 98)	98	9	6	2	1	0	0	0	0	0	0

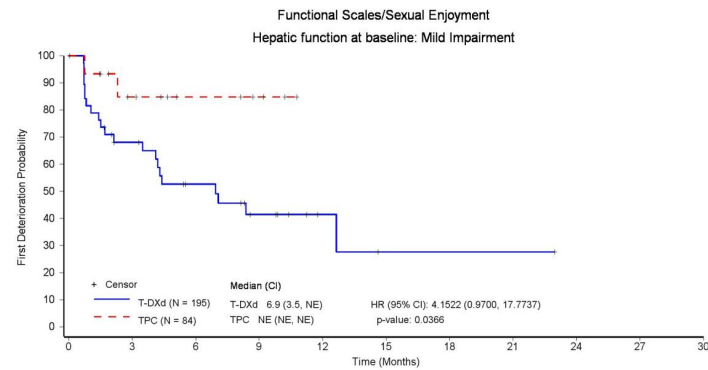
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:19; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCQR45\_FD\_4\_FAS.rtf



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Patients still at risk:

T-DXd (N = 195)	195	23	15	9	3	1	1	1	0	0	0
TPC (N = 84)	84	9	5	3	0	0	0	0	0	0	0

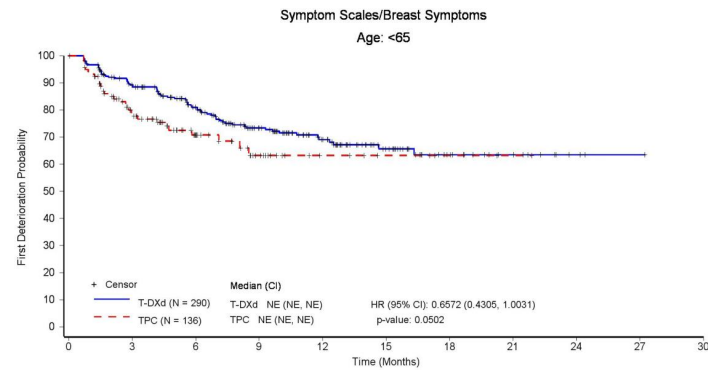
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

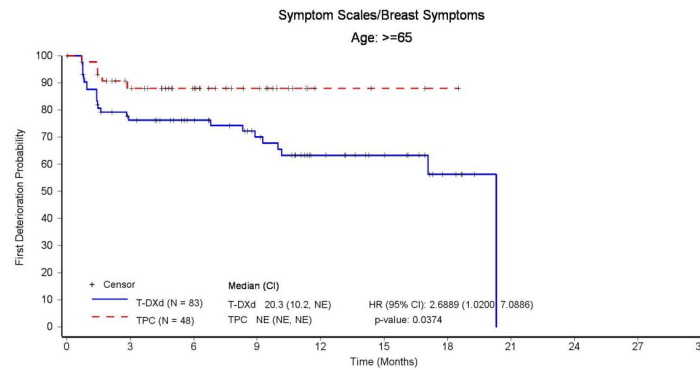
	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 290)	290	223	170	124	77	42	21	12	3	1	0
TPC (N = 136)	136	73	36	17	7	4	2	1	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:19; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCQR45\_FD\_4\_FAS.rtf

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Patients still at risk:

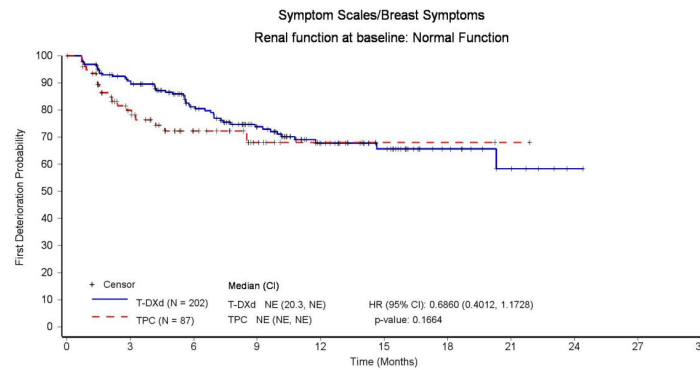
T-DXd (N = 83)	83	51	42	32	20	14	5	0	0	0	0
TPC (N = 48)	48	33	22	13	3	2	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:19; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCQR45\_FD\_4\_FAS.rtf

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Patients still at risk:

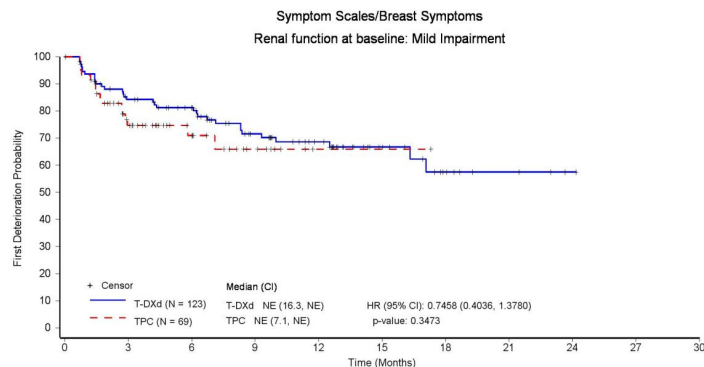
	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 202)	202	159	116	84	48	31	14	7	1	0	0
TPC (N = 87)	87	46	23	11	5	2	2	1	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:19; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCQR45\_FD\_4\_FAS.rtf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 123)	123	87	74	52	38	18	8	4	1	0	0
TPC (N = 69)	69	35	19	8	1	1	0	0	0	0	0

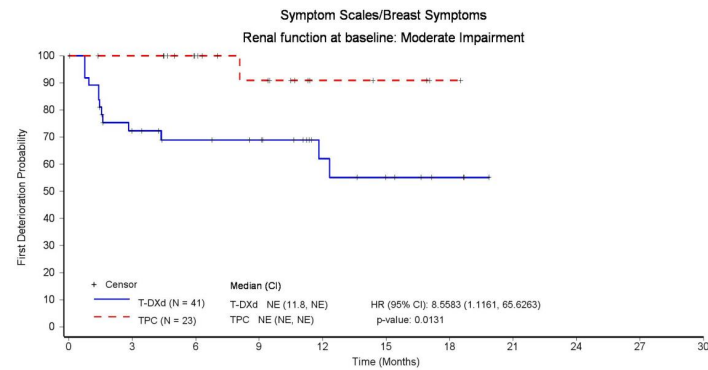
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.3.9.4 - EORTC QLQ-BR45 - First deterioration - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

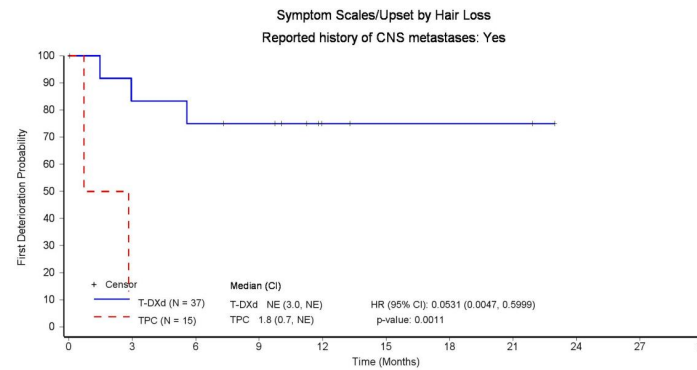
	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 41)	41	23	19	17	9	6	3	0	0	0	0
TPC (N = 23)	23	21	14	10	4	3	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

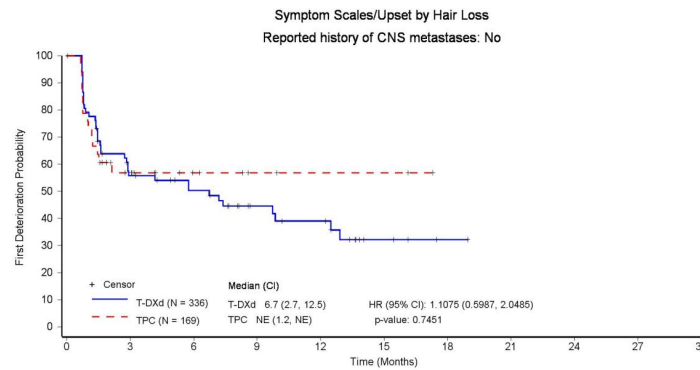
	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 37)	37	10	9	8	3	2	2	2	0	0	0
TPC (N = 15)	15	0	0	0	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:19; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCQR45\_FD\_4\_FAS.rtf

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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 336)	336	34	27	16	13	4	1	0	0	0	0
TPC (N = 169)	169	14	6	3	2	2	0	0	0	0	0

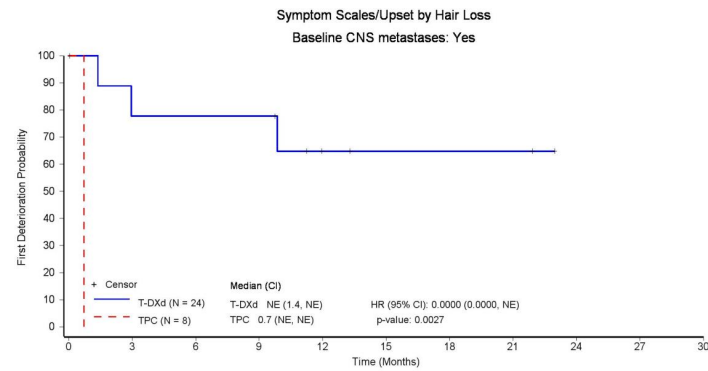
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

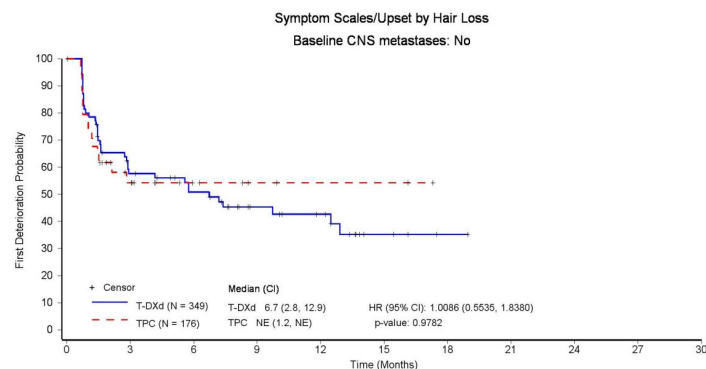
	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 24)	24	7	7	7	3	2	2	2	0	0	0
TPC (N = 8)	8	0	0	0	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:19; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCQR45\_FD\_4\_FAS.rtf

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Patients still at risk:

T-DXd (N = 349)	349	37	29	17	13	4	1	0	0	0	0
TPC (N = 176)	176	14	6	3	2	2	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:19; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCQR45\_FD\_4\_FAS.rtf

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DE.T.3.10.1 - EORTC QLQ-BR45 - Definitive deterioration - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Functional Scales/Body Image

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	116 (31.1)	67 (36.4)	
Number of subjects censored, n (%)	257 (68.9)	117 (63.6)	
Median time to first event (months) [a]	20.1	9.5	
95% Confidence Interval	[16.3, NE]	[5.9, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.5769
95% Confidence Interval			[0.4224, 0.7879]
p-value			0.0005
Stratified log-rank p-value [c]			0.0004

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Functional Scales/Sexual Functioning

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	70 (18.8)	31 (16.8)	
Number of subjects censored, n (%)	303 (81.2)	153 (83.2)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.8321 [0.5411, 1.2795] 0.4024
Stratified log-rank p-value [c]			0.3988

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Functional Scales/Sexual Enjoyment

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	21 (5.6)	4 (2.2)	
Number of subjects censored, n (%)	352 (94.4)	180 (97.8)	
Median time to first event (months) [a] 95% Confidence Interval	NE [11.2, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.7769 [0.5847, 5.3993] 0.3107
Stratified log-rank p-value [c]			0.3064

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Functional Scales/Future Perspective

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	95 (25.5)	44 (23.9)	
Number of subjects censored, n (%)	278 (74.5)	140 (76.1)	
Median time to first event (months) [a] 95% Confidence Interval	NE [20.1, NE]	NE [11.1, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.7659 [0.5308, 1.1051] 0.1539
Stratified log-rank p-value [c]			0.1531

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Symptom Scales/Systemic Therapy Side Effects

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	109 (29.2)	57 (31.0)	
Number of subjects censored, n (%)	264 (70.8)	127 (69.0)	
Median time to first event (months) [a]	22.8	NE	
95% Confidence Interval	[22.3, NE]	[7.0, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.7155
95% Confidence Interval			[0.5154, 0.9934]
p-value			0.0456
Stratified log-rank p-value [c]			0.0430

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Symptom Scales/Breast Symptoms

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	62 (16.6)	22 (12.0)	
Number of subjects censored, n (%)	311 (83.4)	162 (88.0)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.8812 [0.5347, 1.4524] 0.6200
Stratified log-rank p-value [c]			0.6177

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Symptom Scales/Arm Symptoms

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	67 (18.0)	35 (19.0)	
Number of subjects censored, n (%)	306 (82.0)	149 (81.0)	
Median time to first event (months) [a]	NE	17.3	
95% Confidence Interval	[NE, NE]	[12.3, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.5696
95% Confidence Interval			[0.3720, 0.8723]
p-value			0.0096
Stratified log-rank p-value [c]			0.0085

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Symptom Scales/Upset by Hair Loss

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	32 (8.6)	11 (6.0)	
Number of subjects censored, n (%)	341 (91.4)	173 (94.0)	
Median time to first event (months) [a] 95% Confidence Interval	NE [7.4, NE]	NE [6.0, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.8309 [0.4012, 1.7206] 0.6179
Stratified log-rank p-value [c]			0.6255

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.8457
HER2 IHC 1+	214	67 (31.3)	147 (68.7)	20.1 (14.1, NE)	107	38 (35.5)	69 (64.5)	9.8 (5.6, NE)	0.5942 (0.3956, 0.8923) 0.0121	0.0112	
HER2 IHC 2+/ISH Negative	159	49 (30.8)	110 (69.2)	21.9 (14.9, NE)	77	29 (37.7)	48 (62.3)	9.2 (4.5, NE)	0.5362 (0.3340, 0.8609) 0.0099	0.0086	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.1689
1	221	77 (34.8)	144 (65.2)	20.1 (12.8, NE)	100	38 (38.0)	62 (62.0)	14.0 (5.6, NE)	0.6998 (0.4717, 1.0382) 0.0761	0.0737
>=2	151	39 (25.8)	112 (74.2)	21.9 (20.1, NE)	83	29 (34.9)	54 (65.1)	9.5 (4.3, NE)	0.4017 (0.2429, 0.6644) 0.0004	0.0002

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Prior CDK4/6											
Yes	235	70 (29.8)	165 (70.2)	20.1 (20.1, NE)	118	38 (32.2)	80 (67.8)	9.8 (5.9, NE)	0.6561 (0.4392, 0.9802)	0.0371	0.4986
No	98	34 (34.7)	64 (65.3)	20.1 (12.8, NE)	48	21 (43.8)	27 (56.3)	9.5 (3.9, 16.9)	0.4792 (0.2727, 0.8423)	0.0090	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Age										0.0080
<65	290	87 (30.0)	203 (70.0)	20.1 (20.1, NE)	136	56 (41.2)	80 (58.8)	6.1 (4.3, 9.8)	0.4487 (0.3176, 0.6339)	<0.0001
>=65	83	29 (34.9)	54 (65.1)	21.9 (10.8, NE)	48	11 (22.9)	37 (77.1)	16.9 (16.9, NE)	1.2472 (0.6161, 2.5249)	0.5395

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7814
<75	359	113 (31.5)	246 (68.5)	20.1 (20.1, NE)	175	63 (36.0)	112 (64.0)	9.2 (5.9, NE)	0.5747 (0.4190, 0.7884) 0.0006	0.0005	
>=75	14	3 (21.4)	11 (78.6)	14.8 (14.1, NE)	9	4 (44.4)	5 (55.6)	16.9 (1.4, 16.9)	0.4387 (0.0965, 1.9945) 0.2862	0.2735	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.2623
White	176	44 (25.0)	132 (75.0)	NE (20.1, NE)	91	31 (34.1)	60 (65.9)	9.2 (5.1, NE)	0.5137 (0.3212, 0.8216) 0.0054	0.0046	
Non-White	197	72 (36.5)	125 (63.5)	16.3 (12.8, 24.2)	92	35 (38.0)	57 (62.0)	9.8 (4.4, NE)	0.6344 (0.4195, 0.9593) 0.0310	0.0295	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.3068
Asia	147	62 (42.2)	85 (57.8)	14.9 (12.5, 21.9)	66	27 (40.9)	39 (59.1)	9.8 (4.4, NE)	0.6444 (0.4053, 1.0245) 0.0632	0.0610	
North America	60	10 (16.7)	50 (83.3)	NE (10.8, NE)	33	10 (30.3)	23 (69.7)	5.9 (2.9, NE)	0.3254 (0.1304, 0.8120) 0.0161	0.0116	
Europe + Israel	166	44 (26.5)	122 (73.5)	NE (20.1, NE)	85	30 (35.3)	55 (64.7)	9.5 (5.6, NE)	0.5736 (0.3581, 0.9189) 0.0208	0.0187	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.2858
0	200	62 (31.0)	138 (69.0)	20.1 (16.3, NE)	105	39 (37.1)	66 (62.9)	9.5 (4.3, NE)	0.4965 (0.3290, 0.7492) 0.0009	0.0007	
1	173	54 (31.2)	119 (68.8)	21.9 (12.8, 24.2)	79	28 (35.4)	51 (64.6)	9.2 (5.9, NE)	0.6936 (0.4358, 1.1040) 0.1229	0.1198	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.1155
0	60	21 (35.0)	39 (65.0)	14.8 (8.8, 21.9)	34	13 (38.2)	21 (61.8)	5.9 (2.9, NE)	0.5855 (0.2845, 1.2050) 0.1461	0.1411
1	108	35 (32.4)	73 (67.6)	20.1 (9.6, NE)	51	18 (35.3)	33 (64.7)	14.0 (5.9, NE)	0.8344 (0.4708, 1.4788) 0.5353	0.5318
2	115	29 (25.2)	86 (74.8)	20.1 (20.1, NE)	54	23 (42.6)	31 (57.4)	5.9 (2.7, NE)	0.3365 (0.1885, 0.6006) 0.0002	0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	31 (34.4)	59 (65.6)	24.2 (12.8, NE)	45	13 (28.9)	32 (71.1)	9.2 (4.4, NE)	0.7018 (0.3591, 1.3718) 0.3005	0.2967

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Functional Scales/Body Image

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.6241
PD	174	46 (26.4)	128 (73.6)	20.1 (16.3, NE)	85	27 (31.8)	58 (68.2)	9.8 (5.1, NE)	0.5632 (0.3452, 0.9188) 0.0215	0.0197	
PR	48	18 (37.5)	30 (62.5)	14.8 (10.8, 24.2)	22	9 (40.9)	13 (59.1)	4.3 (2.9, NE)	0.4004 (0.1720, 0.9321) 0.0338	0.0284	
SD	82	30 (36.6)	52 (63.4)	21.9 (13.0, NE)	55	20 (36.4)	35 (63.6)	14.0 (5.9, NE)	0.8077 (0.4552, 1.4334) 0.4656	0.4627	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Functional Scales/Body Image

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.1826
Yes	37	14 (37.8)	23 (62.2)	21.9 (6.0, NE)	15	3 (20.0)	12 (80.0)	NE (2.9, NE)	1.1434 (0.3218, 4.0628)	0.8386
No	336	102 (30.4)	234 (69.6)	20.1 (16.3, NE)	169	64 (37.9)	105 (62.1)	9.5 (5.9, 16.9)	0.5362 (0.3892, 0.7388)	0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.4526
Yes	24	11 (45.8)	13 (54.2)	13.0 (5.8, NE)	8	3 (37.5)	5 (62.5)	5.9 (1.4, NE)	0.7553 (0.2054, 2.7772) 0.6727	0.6718	
No	349	105 (30.1)	244 (69.9)	20.1 (20.1, NE)	176	64 (36.4)	112 (63.6)	9.5 (5.9, NE)	0.5575 (0.4055, 0.7665) 0.0003	0.0003	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.1443
Normal Function	202	59 (29.2)	143 (70.8)	NE (21.9, NE)	87	36 (41.4)	51 (58.6)	5.9 (3.9, 14.0)	0.4602 (0.3008, 0.7039) 0.0003	0.0002	
Mild Impairment	123	40 (32.5)	83 (67.5)	20.1 (14.1, NE)	69	23 (33.3)	46 (66.7)	NE (4.3, NE)	0.5186 (0.3022, 0.8899) 0.0172	0.0157	
Moderate Impairment	41	13 (31.7)	28 (68.3)	20.1 (11.2, 20.1)	23	7 (30.4)	16 (69.6)	16.9 (5.9, NE)	1.0946 (0.4300, 2.7860) 0.8496	0.8518	

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.7017
Normal Function	170	57 (33.5)	113 (66.5)	21.9 (14.8, NE)	98	40 (40.8)	58 (59.2)	9.5 (4.3, 16.9)	0.5287 (0.3485, 0.8020) 0.0027	0.0023
Mild Impairment	195	57 (29.2)	138 (70.8)	20.1 (14.1, NE)	84	27 (32.1)	57 (67.9)	9.2 (5.1, NE)	0.6031 (0.3780, 0.9622) 0.0339	0.0324

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1046
Yes	332	101 (30.4)	231 (69.6)	20.1 (16.3, NE)	157	51 (32.5)	106 (67.5)	9.8 (8.6, NE)	0.6459 (0.4582, 0.9106) 0.0126	0.0118	
No	41	15 (36.6)	26 (63.4)	NE (9.0, NE)	27	16 (59.3)	11 (40.7)	4.2 (1.7, 5.9)	0.3262 (0.1549, 0.6868) 0.0032	0.0020	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (IXRS)										0.2241
Positive	331	104 (31.4)	227 (68.6)	20.1 (16.3, NE)	163	56 (34.4)	107 (65.6)	9.8 (6.1, NE)	0.6173 (0.4431, 0.8599)	0.0039
Negative	42	12 (28.6)	30 (71.4)	21.9 (8.8, NE)	21	11 (52.4)	10 (47.6)	4.2 (1.5, NE)	0.3339 (0.1396, 0.7988)	0.0098

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (derived)										0.6079
Positive	333	103 (30.9)	230 (69.1)	20.1 (16.3, NE)	166	59 (35.5)	107 (64.5)	9.5 (5.9, NE)	0.5876 (0.4237, 0.8148)	0.0014
Negative	40	13 (32.5)	27 (67.5)	21.9 (8.8, NE)	18	8 (44.4)	10 (55.6)	5.9 (1.4, NE)	0.4443 (0.1764, 1.1188)	0.0772

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.0700
HER2 IHC 1+	214	41 (19.2)	173 (80.8)	NE (NE, NE)	107	13 (12.1)	94 (87.9)	NE (NE, NE)	1.2322 (0.6556, 2.3159) 0.5167	0.5181
HER2 IHC 2+/ISH Negative	159	29 (18.2)	130 (81.8)	NE (NE, NE)	77	18 (23.4)	59 (76.6)	NE (NE, NE)	0.5808 (0.3204, 1.0525) 0.0732	0.0698

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.1332
1	221	45 (20.4)	176 (79.6)	NE (NE, NE)	100	14 (14.0)	86 (86.0)	NE (NE, NE)	1.1610 (0.6354, 2.1214) 0.6273	0.6245
>=2	151	25 (16.6)	126 (83.4)	NE (20.0, NE)	83	17 (20.5)	66 (79.5)	NE (NE, NE)	0.5925 (0.3146, 1.1157) 0.1050	0.1011

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.1498
Yes	235	43 (18.3)	192 (81.7)	NE (NE, NE)	118	22 (18.6)	96 (81.4)	NE (NE, NE)	0.6954 (0.4128, 1.1716) 0.1723	0.1695	
No	98	20 (20.4)	78 (79.6)	NE (NE, NE)	48	5 (10.4)	43 (89.6)	NE (NE, NE)	1.6759 (0.6251, 4.4930) 0.3048	0.3000	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0836
<65	290	58 (20.0)	232 (80.0)	NE (NE, NE)	136	28 (20.6)	108 (79.4)	NE (NE, NE)	0.6933 (0.4389, 1.0953)	0.1136	
>=65	83	12 (14.5)	71 (85.5)	NE (20.0, NE)	48	3 (6.3)	45 (93.8)	NE (NE, NE)	2.1193 (0.5912, 7.5976)	0.2382	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Age											
<75	359	69 (19.2)	290 (80.8)	NE (NE, NE)	175	30 (17.1)	145 (82.9)	NE (NE, NE)	0.8357 (0.5415, 1.2898)	0.4153	0.9803
>=75	14	1 (7.1)	13 (92.9)	NE (NE, NE)	9	1 (11.1)	8 (88.9)	NE (0.7, NE)	0.7071 (0.0442, 11.3185)	0.8055	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.0454
White	176	38 (21.6)	138 (78.4)	NE (20.0, NE)	91	22 (24.2)	69 (75.8)	NE (8.1, NE)	0.5972 (0.3494, 1.0207) 0.0594	0.0571	
Non-White	197	32 (16.2)	165 (83.8)	NE (NE, NE)	92	8 (8.7)	84 (91.3)	NE (NE, NE)	1.5883 (0.7289, 3.4610) 0.2444	0.2376	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.3052
Asia	147	21 (14.3)	126 (85.7)	NE (NE, NE)	66	5 (7.6)	61 (92.4)	NE (NE, NE)	1.5704 (0.5883, 4.1919) 0.3676	0.3587	
North America	60	8 (13.3)	52 (86.7)	NE (NE, NE)	33	6 (18.2)	27 (81.8)	NE (4.5, NE)	0.5694 (0.1957, 1.6561) 0.3012	0.2933	
Europe + Israel	166	41 (24.7)	125 (75.3)	NE (20.0, NE)	85	20 (23.5)	65 (76.5)	NE (NE, NE)	0.7595 (0.4413, 1.3073) 0.3207	0.3205	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.7423
0	200	43 (21.5)	157 (78.5)	NE (NE, NE)	105	20 (19.0)	85 (81.0)	NE (NE, NE)	0.7972 (0.4658, 1.3644) 0.4084	0.4128	
1	173	27 (15.6)	146 (84.4)	NE (NE, NE)	79	11 (13.9)	68 (86.1)	NE (NE, NE)	0.9852 (0.4873, 1.9919) 0.9668	0.9626	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.1046
0	60	11 (18.3)	49 (81.7)	NE (NE, NE)	34	8 (23.5)	26 (76.5)	NE (3.4, NE)	0.5937 (0.2376, 1.4838)	0.2601
1	108	24 (22.2)	84 (77.8)	NE (18.6, NE)	51	5 (9.8)	46 (90.2)	NE (NE, NE)	2.0151 (0.7645, 5.3118)	0.1484
2	115	22 (19.1)	93 (80.9)	NE (NE, NE)	54	9 (16.7)	45 (83.3)	NE (8.1, NE)	0.8259 (0.3757, 1.8157)	0.6261

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	13 (14.4)	77 (85.6)	NE (NE, NE)	45	9 (20.0)	36 (80.0)	NE (NE, NE)	0.5114 (0.2157, 1.2127) 0.1280	0.1204

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.1555
PD	174	39 (22.4)	135 (77.6)	NE (18.6, NE)	85	17 (20.0)	68 (80.0)	NE (NE, NE)	0.8134 (0.4565, 1.4492) 0.4834	0.4825	
PR	48	4 (8.3)	44 (91.7)	NE (NE, NE)	22	4 (18.2)	18 (81.8)	NE (3.1, NE)	0.2264 (0.0545, 0.9394) 0.0408	0.0263	
SD	82	14 (17.1)	68 (82.9)	NE (20.0, NE)	55	6 (10.9)	49 (89.1)	NE (NE, NE)	1.3572 (0.5170, 3.5630) 0.5351	0.5343	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.4704
Yes	37	7 (18.9)	30 (81.1)	NE (NE, NE)	15	3 (20.0)	12 (80.0)	NE (0.9, NE)	0.4753 (0.1150, 1.9642)	0.2948
No	336	63 (18.8)	273 (81.3)	NE (NE, NE)	169	28 (16.6)	141 (83.4)	NE (NE, NE)	0.8934 (0.5697, 1.4008)	0.6226

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.4819
Yes	24	4 (16.7)	20 (83.3)	NE (NE, NE)	8	2 (25.0)	6 (75.0)	NE (0.9, NE)	0.3406 (0.0538, 2.1544)	0.2312
No	349	66 (18.9)	283 (81.1)	NE (NE, NE)	176	29 (16.5)	147 (83.5)	NE (NE, NE)	0.8945 (0.5755, 1.3902)	0.6200

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.3418
Normal Function	202	40 (19.8)	162 (80.2)	NE (NE, NE)	87	19 (21.8)	68 (78.2)	NE (NE, NE)	0.6492 (0.3736, 1.1282) 0.1255	0.1215	
Mild Impairment	123	26 (21.1)	97 (78.9)	NE (20.0, NE)	69	9 (13.0)	60 (87.0)	NE (NE, NE)	1.1658 (0.5390, 2.5218) 0.6967	0.6975	
Moderate Impairment	41	4 (9.8)	37 (90.2)	NE (NE, NE)	23	2 (8.7)	21 (91.3)	NE (NE, NE)	1.2821 (0.2344, 7.0136) 0.7744	0.7739	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.4437
Normal Function	170	35 (20.6)	135 (79.4)	NE (NE, NE)	98	21 (21.4)	77 (78.6)	NE (NE, NE)	0.7748 (0.4491, 1.3369)	0.3556	
Mild Impairment	195	35 (17.9)	160 (82.1)	NE (20.0, NE)	84	10 (11.9)	74 (88.1)	NE (NE, NE)	1.0584 (0.5191, 2.1583)	0.8734	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.8431
Yes	332	58 (17.5)	274 (82.5)	NE (NE, NE)	157	24 (15.3)	133 (84.7)	NE (NE, NE)	0.8483 (0.5243, 1.3725) 0.5027	0.5016	
No	41	12 (29.3)	29 (70.7)	NE (6.9, NE)	27	7 (25.9)	20 (74.1)	NE (4.5, NE)	1.0491 (0.4118, 2.6723) 0.9200	0.9227	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.5550
Positive	331	63 (19.0)	268 (81.0)	NE (NE, NE)	163	26 (16.0)	137 (84.0)	NE (NE, NE)	0.8980 (0.5659, 1.4249)	0.6478	0.6468
Negative	42	7 (16.7)	35 (83.3)	NE (NE, NE)	21	5 (23.8)	16 (76.2)	NE (3.4, NE)	0.6219 (0.1943, 1.9904)	0.4199	0.4236

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.6594
Positive	333	63 (18.9)	270 (81.1)	NE (NE, NE)	166	27 (16.3)	139 (83.7)	NE (NE, NE)	0.8921 (0.5658, 1.4066)	0.6213	
Negative	40	7 (17.5)	33 (82.5)	NE (10.6, NE)	18	4 (22.2)	14 (77.8)	NE (1.6, NE)	0.5557 (0.1543, 2.0019)	0.3634	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.0054
HER2 IHC 1+	214	9 (4.2)	205 (95.8)	NE (10.9, NE)	107	4 (3.7)	103 (96.3)	NE (0.9, NE)	0.6410 (0.1869, 2.1981)	0.4819
HER2 IHC 2+/ISH Negative	159	12 (7.5)	147 (92.5)	NE (7.1, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE)	0.0240

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.3640
1	221	11 (5.0)	210 (95.0)	NE (11.2, NE)	100	3 (3.0)	97 (97.0)	NE (NE, NE)	1.3592 (0.3745, 4.9327) 0.6407	0.6304
>=2	151	10 (6.6)	141 (93.4)	NE (4.1, NE)	83	1 (1.2)	82 (98.8)	NE (NE, NE)	3.8462 (0.4827, 30.6437) 0.2033	0.1713

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Prior CDK4/6											
Yes	235	14 (6.0)	221 (94.0)	NE (NE, NE)	118	2 (1.7)	116 (98.3)	NE (NE, NE)	2.3340 (0.5262, 10.3527) 0.2648	0.2493	0.9379
No	98	5 (5.1)	93 (94.9)	NE (1.7, NE)	48	1 (2.1)	47 (97.9)	NE (0.8, NE)	2.0777 (0.2386, 18.0902) 0.5078	0.4904	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5973
<65	290	18 (6.2)	272 (93.8)	NE (11.2, NE)	136	3 (2.2)	133 (97.8)	NE (NE, NE)	2.2420 (0.6527, 7.7015) 0.1997	0.1871	
>=65	83	3 (3.6)	80 (96.4)	NE (2.1, NE)	48	1 (2.1)	47 (97.9)	NE (0.8, NE)	0.7944 (0.0702, 8.9933) 0.8525	0.8522	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											
<75	359	21 (5.8)	338 (94.2)	NE (11.2, NE)	175	4 (2.3)	171 (97.7)	NE (NE, NE)	1.9870 (0.6742, 5.8561) 0.2131	0.2014	NE
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Race										0.0614
White	176	12 (6.8)	164 (93.2)	NE (8.8, NE)	91	1 (1.1)	90 (98.9)	NE (NE, NE)	5.2332 (0.6763, 40.4921) 0.1129	0.0769
Non-White	197	9 (4.6)	188 (95.4)	NE (10.9, NE)	92	3 (3.3)	89 (96.7)	NE (0.8, NE)	0.6952 (0.1862, 2.5948) 0.5885	0.6076

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.1656
Asia	147	5 (3.4)	142 (96.6)	11.2 (0.8, NE)	66	0	66 (100)	NE (NE, NE)	NE (NE, NE) 0.9972	0.2248	
North America	60	5 (8.3)	55 (91.7)	NE (2.1, NE)	33	0	33 (100)	NE (NE, NE)	NE (NE, NE) 0.9960	0.2710	
Europe + Israel	166	11 (6.6)	155 (93.4)	NE (NE, NE)	85	4 (4.7)	81 (95.3)	NE (NE, NE)	1.2172 (0.3830, 3.8679) 0.7390	0.7324	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.8061
0	200	12 (6.0)	188 (94.0)	NE (8.8, NE)	105	3 (2.9)	102 (97.1)	NE (NE, NE)	1.7839 (0.4946, 6.4347) 0.3765	0.3641	
1	173	9 (5.2)	164 (94.8)	NE (6.9, NE)	79	1 (1.3)	78 (98.7)	NE (NE, NE)	2.4851 (0.3083, 20.0327) 0.3926	0.3775	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1532
0	60	4 (6.7)	56 (93.3)	10.9 (1.1, NE)	34	1 (2.9)	33 (97.1)	NE (0.9, NE)	2.3033 (0.2567, 20.6683) 0.4561	0.4432	
1	108	7 (6.5)	101 (93.5)	NE (4.3, NE)	51	3 (5.9)	48 (94.1)	NE (0.8, NE)	0.7781 (0.2004, 3.0209) 0.7170	0.7445	
2	115	7 (6.1)	108 (93.9)	NE (8.8, NE)	54	0	54 (100)	NE (NE, NE)	NE (NE, NE) 0.9951	0.1626	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	3 (3.3)	87 (96.7)	NE (3.6, NE)	45	0	45 (100)	NE (NE, NE)	NE (NE, NE) 0.9968	0.2994	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.1623
PD	174	10 (5.7)	164 (94.3)	NE (10.9, NE)	85	3 (3.5)	82 (96.5)	NE (NE, NE)	1.4273 (0.3841, 5.3034) 0.5953	0.5921
PR	48	2 (4.2)	46 (95.8)	NE (0.8, NE)	22	0	22 (100)	NE (NE, NE)	NE 0.9979	0.2649
SD	82	6 (7.3)	76 (92.7)	NE (2.1, NE)	55	0	55 (100)	NE (NE, NE)	NE 0.9965	0.0900

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.3733
Yes	37	3 (8.1)	34 (91.9)	NE (1.6, NE)	15	0	15 (100)	NE (NE, NE)	NE (NE, NE) 0.9975	0.5017	
No	336	18 (5.4)	318 (94.6)	NE (11.2, NE)	169	4 (2.4)	165 (97.6)	NE (NE, NE)	1.7618 (0.5881, 5.2779) 0.3117	0.3012	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											NE
Yes	24	1 (4.2)	23 (95.8)	NE (1.6, NE)	8	0	8 (100)	NE (NE, NE)	NE (NE, NE)		
No	349	20 (5.7)	329 (94.3)	NE (11.2, NE)	176	4 (2.3)	172 (97.7)	NE (NE, NE)	1.9217 (0.6483, 5.6964)	0.2274	0.2387

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.3203
Normal Function	202	15 (7.4)	187 (92.6)	NE (7.1, NE)	87	3 (3.4)	84 (96.6)	NE (NE, NE)	1.6545 (0.4744, 5.7708) 0.4296	0.4234	
Mild Impairment	123	4 (3.3)	119 (96.7)	NE (8.8, NE)	69	0	69 (100)	NE (NE, NE)	NE (NE, NE) 0.9959	0.2215	
Moderate Impairment	41	2 (4.9)	39 (95.1)	11.2 (1.6, NE)	23	1 (4.3)	22 (95.7)	NE (0.8, NE)	0.4714 (0.0283, 7.8580) 0.6004	0.5924	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]	
Hepatic function at baseline										0.1086	
Normal Function	170	6 (3.5)	164 (96.5)	NE (NE, NE)	98	3 (3.1)	95 (96.9)	NE (NE, NE)	0.9244 (0.2246, 3.8050)	0.9144	
Mild Impairment	195	15 (7.7)	180 (92.3)	NE (6.9, NE)	84	1 (1.2)	83 (98.8)	NE (NE, NE)	5.0197 (0.6591, 38.2290)	0.0819	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.3432
Yes	332	17 (5.1)	315 (94.9)	NE (NE, NE)	157	3 (1.9)	154 (98.1)	NE (NE, NE)	2.6345 (0.7702, 9.0117) 0.1226	0.1058	
No	41	4 (9.8)	37 (90.2)	NE (8.8, NE)	27	1 (3.7)	26 (96.3)	NE (0.9, NE)	0.1818 (0.0096, 3.4390) 0.2557	0.2126	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (IXRS)										0.8257
Positive	331	18 (5.4)	313 (94.6)	NE (NE, NE)	163	3 (1.8)	160 (98.2)	NE (NE, NE)	2.1230 (0.6198, 7.2719) 0.2307	0.2158
Negative	42	3 (7.1)	39 (92.9)	6.2 (1.1, 10.9)	21	1 (4.8)	20 (95.2)	NE (0.9, NE)	1.8227 (0.1645, 20.1957) 0.6247	0.6195

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (derived)										0.8938
Positive	333	19 (5.7)	314 (94.3)	NE (NE, NE)	166	3 (1.8)	163 (98.2)	NE (NE, NE)	2.2707 (0.6666, 7.7349) 0.1897	0.1741
Negative	40	2 (5.0)	38 (95.0)	10.9 (1.1, 10.9)	18	1 (5.6)	17 (94.4)	NE (0.9, NE)	0.8165 (0.0503, 13.2411) 0.8866	0.8864

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.3009
HER2 IHC 1+	214	55 (25.7)	159 (74.3)	NE (17.3, NE)	107	22 (20.6)	85 (79.4)	NE (11.1, NE)	0.8451 (0.5097, 1.4012) 0.5142	0.5134
HER2 IHC 2+/ISH Negative	159	40 (25.2)	119 (74.8)	NE (NE, NE)	77	22 (28.6)	55 (71.4)	NE (6.1, NE)	0.6171 (0.3637, 1.0468) 0.0734	0.0716

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.0644
1	221	60 (27.1)	161 (72.9)	NE (17.3, NE)	100	21 (21.0)	79 (79.0)	NE (10.7, NE)	0.9984 (0.6034, 1.6519) 0.9949	0.9964
>=2	151	35 (23.2)	116 (76.8)	NE (NE, NE)	83	23 (27.7)	60 (72.3)	NE (5.9, NE)	0.5019 (0.2928, 0.8602) 0.0122	0.0106

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6									0.2806
Yes	235	61 (26.0)	174 (74.0) (17.3, NE)	118	24 (20.3)	94 (79.7) (10.7, NE)	0.8683 (0.5371, 1.4038) 0.5645	0.5661	
No	98	25 (25.5)	73 (74.5) (16.6, NE)	48	15 (31.3)	33 (68.8) (7.1, NE)	0.5635 (0.2927, 1.0849) 0.0861	0.0820	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Age										0.2393
<65	290	65 (22.4)	225 (77.6)	NE (NE, NE)	136	30 (22.1)	106 (77.9)	NE (NE, NE)	0.6857 (0.4417, 1.0644) 0.0926	0.0914
>=65	83	30 (36.1)	53 (63.9)	17.3 (10.0, NE)	48	14 (29.2)	34 (70.8)	11.3 (10.7, NE)	0.9806 (0.5142, 1.8703) 0.9526	0.9529

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Age										0.2513
<75	359	89 (24.8)	270 (75.2)	NE (20.1, NE)	175	41 (23.4)	134 (76.6)	NE (10.7, NE)	0.7231 (0.4963, 1.0535) 0.0913	0.0905
>=75	14	6 (42.9)	8 (57.1)	14.1 (4.2, NE)	9	3 (33.3)	6 (66.7)	11.3 (3.8, NE)	1.3976 (0.3454, 5.6551) 0.6388	0.6372

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Race										0.5019
White	176	31 (17.6)	145 (82.4)	NE (NE, NE)	91	17 (18.7)	74 (81.3)	NE (11.1, NE)	0.6636 (0.3627, 1.2140) 0.1833	0.1808
Non-White	197	64 (32.5)	133 (67.5)	20.1 (16.6, NE)	92	27 (29.3)	65 (70.7)	11.3 (9.0, NE)	0.7816 (0.4952, 1.2336) 0.2899	0.2889

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Region										0.1654
Asia	147	46 (31.3)	101 (68.7)	NE (17.3, NE)	66	24 (36.4)	42 (63.6)	10.7 (6.1, NE)	0.6048 (0.3665, 0.9978) 0.0490	0.0472
North America	60	9 (15.0)	51 (85.0)	NE (NE, NE)	33	7 (21.2)	26 (78.8)	NE (2.1, NE)	0.5659 (0.2086, 1.5353) 0.2635	0.2585
Europe + Israel	166	40 (24.1)	126 (75.9)	NE (17.3, NE)	85	13 (15.3)	72 (84.7)	NE (11.1, NE)	1.1130 (0.5904, 2.0984) 0.7407	0.7409

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	200	55 (27.5)	145 (72.5)	NE (17.3, NE)	105	27 (25.7)	78 (74.3)	NE (9.0, NE)	0.6562 (0.4103, 1.0494)	0.0784	0.4672
1	173	40 (23.1)	133 (76.9)	NE (NE, NE)	79	17 (21.5)	62 (78.5)	NE (11.3, NE)	0.8981 (0.5062, 1.5934)	0.7093	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.4606
0	60	18 (30.0)	42 (70.0)	NE (13.9, NE)	34	9 (26.5)	25 (73.5)	9.0 (5.9, NE)	0.8256 (0.3669, 1.8575)	0.6367	
1	108	21 (19.4)	87 (80.6)	NE (17.3, NE)	51	12 (23.5)	39 (76.5)	NE (11.1, NE)	0.6628 (0.3245, 1.3537)	0.2557	
2	115	29 (25.2)	86 (74.8)	NE (17.3, NE)	54	15 (27.8)	39 (72.2)	10.7 (5.1, NE)	0.4897 (0.2538, 0.9448)	0.0299	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	27 (30.0)	63 (70.0)	NE (16.3, NE)	45	8 (17.8)	37 (82.2)	NE (NE, NE)	1.2639 (0.5696, 2.8043) 0.5647	0.5627

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.4130
PD	174	46 (26.4)	128 (73.6)	20.1 (16.3, NE)	85	15 (17.6)	70 (82.4)	NE (10.7, NE)	1.0153 (0.5610, 1.8375) 0.9599	0.9563	
PR	48	15 (31.3)	33 (68.8)	NE (11.2, NE)	22	7 (31.8)	15 (68.2)	9.0 (3.8, NE)	0.4881 (0.1940, 1.2283) 0.1277	0.1196	
SD	82	21 (25.6)	61 (74.4)	NE (NE, NE)	55	15 (27.3)	40 (72.7)	11.3 (11.1, NE)	0.6992 (0.3563, 1.3721) 0.2982	0.2937	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.5353
Yes	37	7 (18.9)	30 (81.1)	NE (NE, NE)	15	3 (20.0)	12 (80.0)	NE (2.1, NE)	0.5019 (0.1235, 2.0396)	0.3275
No	336	88 (26.2)	248 (73.8)	NE (20.1, NE)	169	41 (24.3)	128 (75.7)	NE (10.7, NE)	0.7626 (0.5230, 1.1120)	0.1580

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.6998
Yes	24	5 (20.8)	19 (79.2)	NE (NE, NE)	8	1 (12.5)	7 (87.5)	NE (4.3, NE)	1.0990 (0.1240, 9.7391) 0.9324	0.9324
No	349	90 (25.8)	259 (74.2)	NE (20.1, NE)	176	43 (24.4)	133 (75.6)	NE (10.7, NE)	0.7368 (0.5090, 1.0664) 0.1054	0.1044

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.6501
Normal Function	202	45 (22.3)	157 (77.7)	NE (NE, NE)	87	17 (19.5)	70 (80.5)	NE (NE, NE)	0.7864 (0.4462, 1.3860) 0.4060	0.4084	
Mild Impairment	123	36 (29.3)	87 (70.7)	20.1 (14.9, NE)	69	20 (29.0)	49 (71.0)	NE (5.9, NE)	0.6282 (0.3571, 1.1048) 0.1065	0.1048	
Moderate Impairment	41	13 (31.7)	28 (68.3)	NE (11.2, NE)	23	7 (30.4)	16 (69.6)	11.3 (7.7, NE)	1.0176 (0.4050, 2.5571) 0.9704	0.9726	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.8575
Normal Function	170	43 (25.3)	127 (74.7)	NE (20.1, NE)	98	24 (24.5)	74 (75.5)	NE (9.0, NE)	0.6847 (0.4114, 1.1396) 0.1451	0.1418
Mild Impairment	195	51 (26.2)	144 (73.8)	NE (17.3, NE)	84	20 (23.8)	64 (76.2)	11.3 (10.7, NE)	0.7687 (0.4543, 1.3008) 0.3271	0.3272

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 15SEP2022 – 12:19; Program name: T3\_EQ5D\_FD\_2\_FAS.sas; Output name: T3\_EORTC BR45\_DD\_2\_FAS.rtf

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline visceral disease										0.7868
Yes	332	85 (25.6)	247 (74.4)	NE (20.1, NE)	157	39 (24.8)	118 (75.2)	NE (11.1, NE)	0.7218 (0.4912, 1.0607) 0.0969	0.0963
No	41	10 (24.4)	31 (75.6)	NE (NE, NE)	27	5 (18.5)	22 (81.5)	9.0 (5.9, NE)	0.9173 (0.3091, 2.7219) 0.8764	0.8745

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (IXRS)										0.9789
Positive	331	85 (25.7)	246 (74.3)	NE (20.1, NE)	163	39 (23.9)	124 (76.1)	NE (11.1, NE)	0.7359 (0.5005, 1.0819) 0.1188	0.1180
Negative	42	10 (23.8)	32 (76.2)	NE (NE, NE)	21	5 (23.8)	16 (76.2)	9.0 (4.5, NE)	0.8185 (0.2772, 2.4164) 0.7168	0.7103

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (derived)										0.7794
Positive	333	85 (25.5)	248 (74.5)	NE (20.1, NE)	166	39 (23.5)	127 (76.5)	NE (11.1, NE)	0.7470 (0.5079, 1.0985) 0.1382	0.1375
Negative	40	10 (25.0)	30 (75.0)	NE (NE, NE)	18	5 (27.8)	13 (72.2)	9.0 (4.5, NE)	0.7151 (0.2428, 2.1060) 0.5429	0.5351

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.3535
HER2 IHC 1+	214	58 (27.1)	156 (72.9)	22.8 (22.3, NE)	107	34 (31.8)	73 (68.2)	NE (7.0, NE)	0.6236 (0.4050, 0.9601) 0.0320	0.0298
HER2 IHC 2+/ISH Negative	159	51 (32.1)	108 (67.9)	NE (22.3, NE)	77	23 (29.9)	54 (70.1)	NE (6.1, NE)	0.8524 (0.5186, 1.4011) 0.5289	0.5236

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.2322
1	221	75 (33.9)	146 (66.1)	22.3 (15.4, NE)	100	34 (34.0)	66 (66.0)	NE (6.7, NE)	0.8157 (0.5416, 1.2283) 0.3293	0.3231
>=2	151	33 (21.9)	118 (78.1)	NE (NE, NE)	83	23 (27.7)	60 (72.3)	NE (6.1, NE)	0.5884 (0.3433, 1.0085) 0.0537	0.0498

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.6065
Yes	235	72 (30.6)	163 (69.4)	22.3 (22.3, NE)	118	38 (32.2)	80 (67.8)	9.5 (5.4, NE)	0.6971 (0.4671, 1.0404) 0.0774	0.0731	
No	98	25 (25.5)	73 (74.5)	NE (NE, NE)	48	15 (31.3)	33 (68.8)	NE (6.1, NE)	0.6252 (0.3284, 1.1902) 0.1528	0.1505	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2140
<65	290	83 (28.6)	207 (71.4)	22.8 (22.3, NE)	136	43 (31.6)	93 (68.4)	NE (6.1, NE)	0.6305 (0.4334, 0.9175) 0.0159	0.0147	
>=65	83	26 (31.3)	57 (68.7)	NE (9.2, NE)	48	14 (29.2)	34 (70.8)	NE (6.7, NE)	1.0970 (0.5722, 2.1030) 0.7803	0.7800	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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[c] Two-sided p-value from unstratified log-rank test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Age										0.0891
<75	359	103 (28.7)	256 (71.3)	22.8 (22.3, NE)	175	55 (31.4)	120 (68.6)	NE (7.0, NE)	0.6767 (0.4853, 0.9434)	0.0198
>=75	14	6 (42.9)	8 (57.1)	9.2 (2.8, NE)	9	2 (22.2)	7 (77.8)	NE (5.0, NE)	2.8605 (0.5747, 14.2375)	0.1795

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.2306
White	176	57 (32.4)	119 (67.6)	22.3 (15.4, NE)	91	26 (28.6)	65 (71.4)	NE (6.2, NE)	0.8724 (0.5451, 1.3963) 0.5696	0.5626	
Non-White	197	52 (26.4)	145 (73.6)	NE (22.8, NE)	92	31 (33.7)	61 (66.3)	NE (5.9, NE)	0.5965 (0.3801, 0.9359) 0.0246	0.0226	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.7920
Asia	147	44 (29.9)	103 (70.1)	NE (22.8, NE)	66	21 (31.8)	45 (68.2)	NE (6.1, NE)	0.7369 (0.4361, 1.2452) 0.2540	0.2503	
North America	60	15 (25.0)	45 (75.0)	22.3 (22.3, NE)	33	10 (30.3)	23 (69.7)	5.0 (3.2, NE)	0.4897 (0.2109, 1.1371) 0.0967	0.0901	
Europe + Israel	166	50 (30.1)	116 (69.9)	NE (15.4, NE)	85	26 (30.6)	59 (69.4)	NE (6.7, NE)	0.8029 (0.4978, 1.2949) 0.3679	0.3596	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.0494
0	200	53 (26.5)	147 (73.5)	NE (22.3, NE)	105	35 (33.3)	70 (66.7)	NE (5.8, NE)	0.5390 (0.3491, 0.8321) 0.0053	0.0046	
1	173	56 (32.4)	117 (67.6)	22.3 (12.2, NE)	79	22 (27.8)	57 (72.2)	NE (6.2, NE)	1.0258 (0.6234, 1.6878) 0.9202	0.9282	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.1834
0	60	21 (35.0)	39 (65.0)	NE (7.8, NE)	34	8 (23.5)	26 (76.5)	NE (5.9, NE)	1.1885 (0.5244, 2.6934) 0.6791	0.6795
1	108	30 (27.8)	78 (72.2)	22.3 (22.3, NE)	51	13 (25.5)	38 (74.5)	NE (9.5, NE)	0.9541 (0.4938, 1.8434) 0.8888	0.8870
2	115	33 (28.7)	82 (71.3)	22.3 (22.3, NE)	54	21 (38.9)	33 (61.1)	5.0 (3.0, NE)	0.4970 (0.2831, 0.8723) 0.0149	0.0127

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	25 (27.8)	65 (72.2)	NE (16.3, NE)	45	15 (33.3)	30 (66.7)	NE (4.4, NE)	0.5808 (0.3022, 1.1164) 0.1031	0.0979

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.2037
PD	174	47 (27.0)	127 (73.0)	NE (22.8, NE)	85	32 (37.6)	53 (62.4)	7.7 (4.2, NE)	0.4946 (0.3130, 0.7817) 0.0026	0.0020
PR	48	15 (31.3)	33 (68.8)	22.3 (22.3, NE)	22	6 (27.3)	16 (72.7)	NE (3.9, NE)	0.7434 (0.2842, 1.9443) 0.5455	0.5401
SD	82	19 (23.2)	63 (76.8)	NE (NE, NE)	55	10 (18.2)	45 (81.8)	NE (NE, NE)	1.0988 (0.5075, 2.3793) 0.8110	0.8162

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.6268
Yes	37	8 (21.6)	29 (78.4)	22.3 (22.3, NE)	15	3 (20.0)	12 (80.0)	NE (0.8, NE)	0.4068 (0.0991, 1.6706) 0.2121	0.1996	
No	336	101 (30.1)	235 (69.9)	NE (22.3, NE)	169	54 (32.0)	115 (68.0)	NE (7.0, NE)	0.7563 (0.5415, 1.0563) 0.1013	0.0973	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.2019
Yes	24	2 (8.3)	22 (91.7)	NE (NE, NE)	8	2 (25.0)	6 (75.0)	NE (0.8, NE)	0.2491 (0.0348, 1.7813)	0.1364
No	349	107 (30.7)	242 (69.3)	22.8 (22.3, NE)	176	55 (31.3)	121 (68.8)	NE (7.0, NE)	0.7555 (0.5435, 1.0503)	0.0918

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.4879
Normal Function	202	58 (28.7)	144 (71.3)	22.3 (22.3, NE)	87	29 (33.3)	58 (66.7)	NE (4.4, NE)	0.6172 (0.3923, 0.9711) 0.0369	0.0338	
Mild Impairment	123	39 (31.7)	84 (68.3)	22.8 (16.3, NE)	69	18 (26.1)	51 (73.9)	NE (6.1, NE)	0.9111 (0.5157, 1.6097) 0.7486	0.7491	
Moderate Impairment	41	12 (29.3)	29 (70.7)	NE (9.2, NE)	23	8 (34.8)	15 (65.2)	NE (5.9, NE)	0.8775 (0.3585, 2.1477) 0.7748	0.7754	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.3787
Normal Function	170	57 (33.5)	113 (66.5)	22.3 (22.3, NE)	98	30 (30.6)	68 (69.4)	NE (6.7, NE)	0.8620 (0.5510, 1.3487) 0.5156	0.5079	
Mild Impairment	195	52 (26.7)	143 (73.3)	NE (22.8, NE)	84	26 (31.0)	58 (69.0)	9.5 (5.4, NE)	0.6124 (0.3795, 0.9883) 0.0446	0.0417	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline visceral disease										0.2579
Yes	332	98 (29.5)	234 (70.5)	22.8 (22.3, NE)	157	46 (29.3)	111 (70.7)	NE (9.5, NE)	0.7788 (0.5466, 1.1098) 0.1666	0.1627
No	41	11 (26.8)	30 (73.2)	NE (10.9, NE)	27	11 (40.7)	16 (59.3)	6.7 (3.0, NE)	0.4502 (0.1905, 1.0642) 0.0690	0.0618

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (IXRS)										0.7797
Positive	331	96 (29.0)	235 (71.0)	22.8 (22.3, NE)	163	50 (30.7)	113 (69.3)	NE (7.7, NE)	0.7160 (0.5064, 1.0123) 0.0586	0.0558
Negative	42	13 (31.0)	29 (69.0)	NE (7.8, NE)	21	7 (33.3)	14 (66.7)	7.0 (4.4, NE)	0.7713 (0.3006, 1.9787) 0.5890	0.5887

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (derived)										0.2583
Positive	333	96 (28.8)	237 (71.2)	22.8 (22.3, NE)	166	53 (31.9)	113 (68.1)	NE (6.7, NE)	0.6796 (0.4837, 0.9549) 0.0260	0.0244
Negative	40	13 (32.5)	27 (67.5)	NE (4.2, NE)	18	4 (22.2)	14 (77.8)	NE (5.9, NE)	1.2711 (0.4082, 3.9577) 0.6790	0.6793

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.6843
HER2 IHC 1+	214	39 (18.2)	175 (81.8)	NE (NE, NE)	107	13 (12.1)	94 (87.9)	NE (NE, NE)	1.0819 (0.5735, 2.0409)	0.8089	
HER2 IHC 2+/ISH Negative	159	23 (14.5)	136 (85.5)	NE (NE, NE)	77	9 (11.7)	68 (88.3)	NE (NE, NE)	0.6754 (0.3081, 1.4808)	0.3248	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.7580
1	221	37 (16.7)	184 (83.3)	NE (NE, NE)	100	12 (12.0)	88 (88.0)	NE (NE, NE)	0.9732 (0.5032, 1.8821) 0.9356	0.9357	
>=2	151	25 (16.6)	126 (83.4)	NE (NE, NE)	83	10 (12.0)	73 (88.0)	NE (NE, NE)	0.7902 (0.3727, 1.6755) 0.5392	0.5385	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.6625
Yes	235	41 (17.4)	194 (82.6)	NE (NE, NE)	118	14 (11.9)	104 (88.1)	NE (NE, NE)	0.9647 (0.5205, 1.7880) 0.9091	0.9087	
No	98	14 (14.3)	84 (85.7)	NE (NE, NE)	48	6 (12.5)	42 (87.5)	NE (NE, NE)	0.7331 (0.2780, 1.9334) 0.5303	0.5289	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Age										0.0175
<65	290	47 (16.2)	243 (83.8)	NE (NE, NE)	136	20 (14.7)	116 (85.3)	NE (NE, NE)	0.6459 (0.3789, 1.1008) 0.1081	0.1056
>=65	83	15 (18.1)	68 (81.9)	NE (17.1, NE)	48	2 (4.2)	46 (95.8)	NE (NE, NE)	3.4694 (0.7832, 15.3678) 0.1014	0.0815

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2732
<75	359	61 (17.0)	298 (83.0)	NE (NE, NE)	175	22 (12.6)	153 (87.4)	NE (NE, NE)	0.8292 (0.5046, 1.3627) 0.4600	0.4588	
>=75	14	1 (7.1)	13 (92.9)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9984	0.3865	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.4963
White	176	23 (13.1)	153 (86.9)	NE (NE, NE)	91	10 (11.0)	81 (89.0)	NE (NE, NE)	0.7264 (0.3393, 1.5553) 0.4105	0.4079	
Non-White	197	39 (19.8)	158 (80.2)	NE (NE, NE)	92	12 (13.0)	80 (87.0)	NE (NE, NE)	1.0174 (0.5278, 1.9613) 0.9588	0.9589	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.7138
Asia	147	30 (20.4)	117 (79.6)	NE (NE, NE)	66	10 (15.2)	56 (84.8)	NE (NE, NE)	0.8615 (0.4163, 1.7827) 0.6878	0.6868	
North America	60	9 (15.0)	51 (85.0)	NE (NE, NE)	33	2 (6.1)	31 (93.9)	NE (NE, NE)	1.8752 (0.3984, 8.8270) 0.4264	0.4174	
Europe + Israel	166	23 (13.9)	143 (86.1)	NE (NE, NE)	85	10 (11.8)	75 (88.2)	NE (NE, NE)	0.7195 (0.3368, 1.5367) 0.3952	0.3929	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.9183
0	200	32 (16.0)	168 (84.0)	NE (NE, NE)	105	11 (10.5)	94 (89.5)	NE (NE, NE)	0.9378 (0.4678, 1.8799)	0.8558 (0.8563)	
1	173	30 (17.3)	143 (82.7)	NE (NE, NE)	79	11 (13.9)	68 (86.1)	NE (NE, NE)	0.8410 (0.4151, 1.7038)	0.6299 (0.6308)	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.4796
0	60	10 (16.7)	50 (83.3)	NE (NE, NE)	34	4 (11.8)	30 (88.2)	NE (7.1, NE)	0.9881 (0.3075, 3.1756)	0.9840
1	108	20 (18.5)	88 (81.5)	NE (NE, NE)	51	5 (9.8)	46 (90.2)	NE (NE, NE)	1.6372 (0.6129, 4.3728)	0.3209
2	115	20 (17.4)	95 (82.6)	NE (NE, NE)	54	8 (14.8)	46 (85.2)	NE (NE, NE)	0.5945 (0.2496, 1.4158)	0.2354

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	12 (13.3)	78 (86.7)	NE (17.1, NE)	45	5 (11.1)	40 (88.9)	NE (NE, NE)	0.5803 (0.1933, 1.7423) 0.3320	0.3269	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.9411
PD	174	30 (17.2)	144 (82.8)	NE (17.1, NE)	85	11 (12.9)	74 (87.1)	NE (NE, NE)	0.7533 (0.3696, 1.5355) 0.4356	0.4344
PR	48	9 (18.8)	39 (81.3)	NE (15.4, NE)	22	2 (9.1)	20 (90.9)	NE (NE, NE)	1.0790 (0.2198, 5.2980) 0.9253	0.9253
SD	82	8 (9.8)	74 (90.2)	NE (NE, NE)	55	5 (9.1)	50 (90.9)	NE (NE, NE)	0.9192 (0.2988, 2.8275) 0.8831	0.8831

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.7180
Yes	37	6 (16.2)	31 (83.8)	NE (13.1, NE)	15	1 (6.7)	14 (93.3)	NE (3.0, NE)	1.1693 (0.1338, 10.2167) 0.8875	0.8874
No	336	56 (16.7)	280 (83.3)	NE (NE, NE)	169	21 (12.4)	148 (87.6)	NE (NE, NE)	0.8766 (0.5262, 1.4603) 0.6130	0.6123

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.9893
Yes	24	4 (16.7)	20 (83.3)	NE (13.1, NE)	8	1 (12.5)	7 (87.5)	NE (3.0, NE)	0.6856 (0.0715, 6.5785)	0.7422
No	349	58 (16.6)	291 (83.4)	NE (NE, NE)	176	21 (11.9)	155 (88.1)	NE (NE, NE)	0.9041 (0.5442, 1.5020)	0.6964

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0056
Normal Function	202	29 (14.4)	173 (85.6)	NE (NE, NE)	87	11 (12.6)	76 (87.4)	NE (NE, NE)	0.6618 (0.3257, 1.3446) 0.2537	0.2508	
Mild Impairment	123	23 (18.7)	100 (81.3)	NE (17.1, NE)	69	10 (14.5)	59 (85.5)	NE (NE, NE)	0.6669 (0.3080, 1.4440) 0.3041	0.3008	
Moderate Impairment	41	9 (22.0)	32 (78.0)	NE (12.3, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9930	0.0209	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.4297
Normal Function	170	27 (15.9)	143 (84.1)	NE (NE, NE)	98	13 (13.3)	85 (86.7)	NE (NE, NE)	0.7403 (0.3761, 1.4571) 0.3842	0.3827	
Mild Impairment	195	34 (17.4)	161 (82.6)	NE (NE, NE)	84	8 (9.5)	76 (90.5)	NE (NE, NE)	1.1211 (0.5132, 2.4490) 0.7744	0.7746	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1455
Yes	332	56 (16.9)	276 (83.1)	NE (NE, NE)	157	17 (10.8)	140 (89.2)	NE (NE, NE)	1.0567 (0.6103, 1.8298) 0.8439	0.8445	
No	41	6 (14.6)	35 (85.4)	NE (17.1, NE)	27	5 (18.5)	22 (81.5)	NE (5.7, NE)	0.2644 (0.0646, 1.0831) 0.0645	0.0497	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.6888
Positive	331	55 (16.6)	276 (83.4)	NE (NE, NE)	163	20 (12.3)	143 (87.7)	NE (NE, NE)	0.8935 (0.5318, 1.5014) 0.6707	0.6697	
Negative	42	7 (16.7)	35 (83.3)	17.1 (11.8, NE)	21	2 (9.5)	19 (90.5)	NE (5.3, NE)	0.6544 (0.1136, 3.7694) 0.6350	0.6329	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.6503
Positive	333	54 (16.2)	279 (83.8)	NE (NE, NE)	166	20 (12.0)	146 (88.0)	NE (NE, NE)	0.8842 (0.5253, 1.4883) 0.6432	0.6424	
Negative	40	8 (20.0)	32 (80.0)	17.1 (11.8, NE)	18	2 (11.1)	16 (88.9)	NE (5.3, NE)	0.7997 (0.1499, 4.2654) 0.7935	0.7931	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.8046
HER2 IHC 1+	214	38 (17.8)	176 (82.2)	NE (NE, NE)	107	18 (16.8)	89 (83.2)	NE (NE, NE)	0.5970 (0.3346, 1.0653) 0.0808	0.0780
HER2 IHC 2+/ISH Negative	159	29 (18.2)	130 (81.8)	NE (NE, NE)	77	17 (22.1)	60 (77.9)	17.3 (12.3, NE)	0.5081 (0.2760, 0.9356) 0.0297	0.0266

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.0401
1	221	46 (20.8)	175 (79.2)	NE (18.6, NE)	100	17 (17.0)	83 (83.0)	NE (17.3, NE)	0.8305 (0.4726, 1.4596) 0.5186	0.5180
>=2	151	21 (13.9)	130 (86.1)	NE (NE, NE)	83	18 (21.7)	65 (78.3)	NE (12.3, NE)	0.2968 (0.1528, 0.5763) 0.0003	0.0002

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Prior CDK4/6											
Yes	235	43 (18.3)	192 (81.7)	NE (NE, NE)	118	19 (16.1)	99 (83.9)	17.3 (17.3, NE)	0.6608 (0.3798, 1.1496)	0.1398	0.2301
No	98	16 (16.3)	82 (83.7)	NE (18.4, NE)	48	12 (25.0)	36 (75.0)	NE (12.3, NE)	0.3437 (0.1590, 0.7427)	0.0046	0.0066

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Age										0.7327
<65	290	57 (19.7)	233 (80.3)	NE (NE, NE)	136	27 (19.9)	109 (80.1)	17.3 (12.3, NE)	0.5492 (0.3438, 0.8774) 0.0122	0.0110
>=65	83	10 (12.0)	73 (88.0)	NE (18.4, NE)	48	8 (16.7)	40 (83.3)	NE (NE, NE)	0.4810 (0.1822, 1.2697) 0.1395	0.1320

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Age											
<75	359	66 (18.4)	293 (81.6)	NE (NE, NE)	175	35 (20.0)	140 (80.0)	17.3 (12.3, NE)	0.5156 (0.3380, 0.7864) 0.0021	0.0018	0.2079
>=75	14	1 (7.1)	13 (92.9)	NE (5.8, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9984	0.4028	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.2565
White	176	29 (16.5)	147 (83.5)	NE (NE, NE)	91	19 (20.9)	72 (79.1)	17.3 (12.3, 17.3)	0.4018 (0.2209, 0.7308) 0.0028	0.0020	
Non-White	197	38 (19.3)	159 (80.7)	NE (NE, NE)	92	16 (17.4)	76 (82.6)	NE (NE, NE)	0.7367 (0.4067, 1.3345) 0.3134	0.3128	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Region										0.7622
Asia	147	32 (21.8)	115 (78.2)	NE (18.6, NE)	66	14 (21.2)	52 (78.8)	NE (NE, NE)	0.7058 (0.3740, 1.3317) 0.2820	0.2807
North America	60	9 (15.0)	51 (85.0)	NE (14.5, NE)	33	4 (12.1)	29 (87.9)	NE (5.8, NE)	0.5349 (0.1549, 1.8465) 0.3223	0.3153
Europe + Israel	166	26 (15.7)	140 (84.3)	NE (NE, NE)	85	17 (20.0)	68 (80.0)	17.3 (12.3, 17.3)	0.4374 (0.2327, 0.8223) 0.0102	0.0084

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.4378
0	200	35 (17.5)	165 (82.5)	NE (NE, NE)	105	20 (19.0)	85 (81.0)	17.3 (12.3, NE)	0.4436 (0.2516, 0.7821) 0.0050	0.0040	
1	173	32 (18.5)	141 (81.5)	NE (NE, NE)	79	15 (19.0)	64 (81.0)	NE (NE, NE)	0.7277 (0.3908, 1.3552) 0.3164	0.3132	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.7101
0	60	15 (25.0)	45 (75.0)	NE (NE, NE)	34	6 (17.6)	28 (82.4)	NE (5.9, NE)	0.9795 (0.3785, 2.5351) 0.9660	0.9634
1	108	17 (15.7)	91 (84.3)	NE (18.6, NE)	51	11 (21.6)	40 (78.4)	17.3 (12.3, 17.3)	0.4818 (0.2207, 1.0517) 0.0668	0.0606
2	115	22 (19.1)	93 (80.9)	NE (NE, NE)	54	11 (20.4)	43 (79.6)	NE (5.4, NE)	0.4788 (0.2230, 1.0283) 0.0590	0.0538

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	13 (14.4)	77 (85.6)	NE (18.4, NE)	45	7 (15.6)	38 (84.4)	NE (NE, NE)	0.4325 (0.1663, 1.1251) 0.0857	0.0780

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.4082
PD	174	29 (16.7)	145 (83.3)	NE (18.6, NE)	85	14 (16.5)	71 (83.5)	NE (NE, NE)	0.6093 (0.3155, 1.1768) 0.1401	0.1368
PR	48	6 (12.5)	42 (87.5)	NE (NE, NE)	22	5 (22.7)	17 (77.3)	NE (3.1, NE)	0.2266 (0.0626, 0.8202) 0.0237	0.0143
SD	82	17 (20.7)	65 (79.3)	NE (18.4, NE)	55	12 (21.8)	43 (78.2)	17.3 (17.3, NE)	0.6243 (0.2942, 1.3247) 0.2197	0.2155

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.4407
Yes	37	6 (16.2)	31 (83.8)	NE (NE, NE)	15	1 (6.7)	14 (93.3)	NE (1.6, NE)	1.1779 (0.1362, 10.1901) 0.8818	0.8761	
No	336	61 (18.2)	275 (81.8)	NE (NE, NE)	169	34 (20.1)	135 (79.9)	17.3 (12.3, NE)	0.5298 (0.3439, 0.8160) 0.0039	0.0034	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.7200
Yes	24	4 (16.7)	20 (83.3)	NE (NE, NE)	8	1 (12.5)	7 (87.5)	NE (1.6, NE)	0.9268 (0.1005, 8.5490)	0.9562
No	349	63 (18.1)	286 (81.9)	NE (NE, NE)	176	34 (19.3)	142 (80.7)	17.3 (12.3, NE)	0.5373 (0.3498, 0.8253)	0.0040

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Renal function at baseline										0.3245
Normal Function	202	32 (15.8)	170 (84.2)	NE (NE, NE)	87	16 (18.4)	71 (81.6)	NE (NE, NE)	0.4670 (0.2513, 0.8676) 0.0160	0.0138
Mild Impairment	123	24 (19.5)	99 (80.5)	NE (18.4, NE)	69	14 (20.3)	55 (79.7)	17.3 (NE, NE)	0.5311 (0.2675, 1.0544) 0.0705	0.0657
Moderate Impairment	41	10 (24.4)	31 (75.6)	NE (11.3, NE)	23	4 (17.4)	19 (82.6)	NE (12.3, NE)	1.1382 (0.3537, 3.6629) 0.8282	0.8281

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.3986
Normal Function	170	34 (20.0)	136 (80.0)	NE (NE, NE)	98	18 (18.4)	80 (81.6)	NE (12.3, NE)	0.6793 (0.3793, 1.2166) 0.1934	0.1909
Mild Impairment	195	32 (16.4)	163 (83.6)	NE (18.6, NE)	84	16 (19.0)	68 (81.0)	17.3 (NE, NE)	0.4414 (0.2361, 0.8252) 0.0104	0.0086

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline visceral disease										0.8132
Yes	332	56 (16.9)	276 (83.1)	NE (NE, NE)	157	28 (17.8)	129 (82.2)	17.3 (12.3, NE)	0.5607 (0.3526, 0.8917) 0.0145	0.0133
No	41	11 (26.8)	30 (73.2)	NE (14.4, NE)	27	7 (25.9)	20 (74.1)	NE (4.5, NE)	0.5651 (0.2080, 1.5356) 0.2631	0.2571

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (IXRS)										0.9134
Positive	331	58 (17.5)	273 (82.5)	NE (NE, NE)	163	30 (18.4)	133 (81.6)	17.3 (12.3, NE)	0.5354 (0.3406, 0.8417)	0.0068
Negative	42	9 (21.4)	33 (78.6)	NE (NE, NE)	21	5 (23.8)	16 (76.2)	NE (3.9, NE)	0.7653 (0.2536, 2.3097)	0.6305

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (derived)										0.7156
Positive	333	58 (17.4)	275 (82.6)	NE (NE, NE)	166	31 (18.7)	135 (81.3)	17.3 (12.3, NE)	0.5236 (0.3345, 0.8196)	0.0047
Negative	40	9 (22.5)	31 (77.5)	NE (7.8, NE)	18	4 (22.2)	14 (77.8)	NE (3.4, NE)	0.8476 (0.2588, 2.7757)	0.7845

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.8975
HER2 IHC 1+	214	18 (8.4)	196 (91.6)	12.9 (3.0, NE)	107	6 (5.6)	101 (94.4)	NE (1.2, NE)	0.9769 (0.3851, 2.4781)	0.9614
HER2 IHC 2+/ISH Negative	159	14 (8.8)	145 (91.2)	NE (6.7, NE)	77	5 (6.5)	72 (93.5)	NE (2.7, NE)	1.0608 (0.3788, 2.9709)	0.9140

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.2876
1	221	23 (10.4)	198 (89.6)	12.5 (2.9, NE)	100	7 (7.0)	93 (93.0)	NE (2.7, NE)	1.4227 (0.6073, 3.3325) 0.4170	0.4144
>=2	151	9 (6.0)	142 (94.0)	NE (9.7, NE)	83	4 (4.8)	79 (95.2)	NE (0.7, NE)	0.5610 (0.1708, 1.8422) 0.3407	0.3321

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.8773
Yes	235	19 (8.1)	216 (91.9)	NE (7.2, NE)	118	7 (5.9)	111 (94.1)	NE (2.7, NE)	0.7798 (0.3212, 1.8930)	0.5780	
No	98	9 (9.2)	89 (90.8)	NE (1.4, NE)	48	4 (8.3)	44 (91.7)	NE (0.7, NE)	0.9003 (0.2769, 2.9271)	0.8618	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											0.6001
<65	290	27 (9.3)	263 (90.7)	12.9 (7.2, NE)	136	7 (5.1)	129 (94.9)	NE (2.1, NE)	1.1241 (0.4859, 2.6001) 0.7846	0.7901	
>=65	83	5 (6.0)	78 (94.0)	NE (2.8, NE)	48	4 (8.3)	44 (91.7)	NE (0.7, NE)	0.8242 (0.2205, 3.0811) 0.7738	0.7853	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											1.0000
<75	359	32 (8.9)	327 (91.1)	NE (7.2, NE)	175	11 (6.3)	164 (93.7)	NE (6.0, NE)	1.0040 (0.5026, 2.0056) 0.9910	0.9916	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Race											0.0791
White	176	11 (6.3)	165 (93.8)	NE (7.2, NE)	91	7 (7.7)	84 (92.3)	NE (1.2, NE)	0.5567 (0.2121, 1.4614) 0.2342	0.2287	
Non-White	197	21 (10.7)	176 (89.3)	12.5 (2.9, NE)	92	4 (4.3)	88 (95.7)	NE (6.0, NE)	1.8383 (0.6270, 5.3891) 0.2672	0.2614	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.1123
Asia	147	15 (10.2)	132 (89.8)	7.4 (1.4, NE)	66	4 (6.1)	62 (93.9)	NE (2.1, NE)	1.7994 (0.5949, 5.4425) 0.2982	0.2935	
North America	60	1 (1.7)	59 (98.3)	NE (4.2, NE)	33	2 (6.1)	31 (93.9)	NE (1.0, NE)	0.1121 (0.0096, 1.3098) 0.0810	0.0385	
Europe + Israel	166	16 (9.6)	150 (90.4)	12.9 (7.2, NE)	85	5 (5.9)	80 (94.1)	NE (1.2, NE)	1.0415 (0.3790, 2.8622) 0.9372	0.9285	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.7389
0	200	15 (7.5)	185 (92.5)	12.9 (1.6, NE)	105	7 (6.7)	98 (93.3)	6.0 (2.1, NE)	0.9959 (0.4007, 2.4752) 0.9929	0.9869	
1	173	17 (9.8)	156 (90.2)	NE (7.2, NE)	79	4 (5.1)	75 (94.9)	NE (0.8, NE)	1.2365 (0.4138, 3.6944) 0.7039	0.6988	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.2134
0	60	4 (6.7)	56 (93.3)	NE (0.7, NE)	34	1 (2.9)	33 (97.1)	NE (0.7, NE)	1.4709 (0.1620, 13.3567) 0.7318	0.7141
1	108	15 (13.9)	93 (86.1)	4.2 (2.8, NE)	51	3 (5.9)	48 (94.1)	NE (0.8, NE)	1.7388 (0.5026, 6.0153) 0.3823	0.3680
2	115	6 (5.2)	109 (94.8)	NE (NE, NE)	54	5 (9.3)	49 (90.7)	NE (0.7, NE)	0.3809 (0.1126, 1.2879) 0.1204	0.1076

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	7 (7.8)	83 (92.2)	NE (6.2, NE)	45	2 (4.4)	43 (95.6)	NE (1.2, NE)	1.1431 (0.2241, 5.8300) 0.8722	0.8721

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.0448
PD	174	15 (8.6)	159 (91.4)	NE (6.2, NE)	85	2 (2.4)	83 (97.6)	NE (NE, NE)	2.5105 (0.5711, 11.0364) 0.2231	0.2080	
PR	48	5 (10.4)	43 (89.6)	12.9 (0.7, NE)	22	0	22 (100)	NE (NE, NE)	NE (NE, NE) 0.9971	0.1591	
SD	82	5 (6.1)	77 (93.9)	NE (2.8, NE)	55	7 (12.7)	48 (87.3)	6.0 (0.8, NE)	0.5018 (0.1541, 1.6336) 0.2522	0.2460	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Reported history of CNS metastases											0.2801
Yes	37	2 (5.4)	35 (94.6)	NE (3.0, NE)	15	1 (6.7)	14 (93.3)	6.0 (NE, NE)	0.2930 (0.0261, 3.2872) 0.3196	0.2902	
No	336	30 (8.9)	306 (91.1)	12.9 (6.2, NE)	169	10 (5.9)	159 (94.1)	NE (2.7, NE)	1.2022 (0.5848, 2.4715) 0.6165	0.6160	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.5853
Yes	24	2 (8.3)	22 (91.7)	NE (1.4, NE)	8	0	8 (100)	NE (NE, NE)	0.9981	0.6270
No	349	30 (8.6)	319 (91.4)	12.9 (6.7, NE)	176	11 (6.3)	165 (93.8)	NE (6.0, NE)	1.0650 (0.5308, 2.1367)	0.8596

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.5997
Normal Function	202	19 (9.4)	183 (90.6)	NE (3.0, NE)	87	3 (3.4)	84 (96.6)	NE (2.1, NE)	1.8132 (0.5339, 6.1581) 0.3401	0.3378	
Mild Impairment	123	11 (8.9)	112 (91.1)	12.5 (2.8, NE)	69	7 (10.1)	62 (89.9)	NE (0.8, NE)	0.7880 (0.3021, 2.0557) 0.6263	0.6317	
Moderate Impairment	41	2 (4.9)	39 (95.1)	NE (0.7, NE)	23	1 (4.3)	22 (95.7)	NE (0.7, NE)	0.5316 (0.0478, 5.9095) 0.6071	0.6012	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.8179
Normal Function	170	16 (9.4)	154 (90.6)	12.9 (2.9, NE)	98	6 (6.1)	92 (93.9)	NE (2.7, NE)	1.0951 (0.4196, 2.8585)	0.8548
Mild Impairment	195	16 (8.2)	179 (91.8)	NE (7.2, NE)	84	5 (6.0)	79 (94.0)	NE (1.2, NE)	0.9656 (0.3518, 2.6503)	0.9434

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 15SEP2022 – 12:19; Program name: T3\_EQ5D\_FD\_2\_FAS.sas; Output name: T3\_EORTCBR45\_DD\_2\_FAS.rtf

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.8640
Yes	332	26 (7.8)	306 (92.2)	NE (7.4, NE)	157	9 (5.7)	148 (94.3)	NE (6.0, NE)	1.0114 (0.4710, 2.1717) 0.9769	0.9772	
No	41	6 (14.6)	35 (85.4)	NE (0.7, NE)	27	2 (7.4)	25 (92.6)	NE (1.2, NE)	1.1065 (0.2227, 5.4972) 0.9015	0.9111	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 15SEP2022 – 12:19; Program name: T3\_EQ5D\_FD\_2\_FAS.sas; Output name: T3\_EORTCBR45\_DD\_2\_FAS.rtf



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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.1118
Positive	331	29 (8.8)	302 (91.2)	NE (7.2, NE)	163	11 (6.7)	152 (93.3)	NE (2.7, NE)	0.8916 (0.4424, 1.7966)	0.7458	
Negative	42	3 (7.1)	39 (92.9)	7.4 (0.7, NE)	21	0	21 (100)	NE (NE, NE)	NE (NE, NE)	0.2446	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 15SEP2022 – 12:19; Program name: T3\_EQ5D\_FD\_2\_FAS.sas; Output name: T3\_EORTC BR45\_DD\_2\_FAS.rf

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.0714
Positive	333	28 (8.4)	305 (91.6)	NE (9.7, NE)	166	11 (6.6)	155 (93.4)	NE (2.7, NE)	0.8659 (0.4280, 1.7517) 0.6887	0.6892	
Negative	40	4 (10.0)	36 (90.0)	7.4 (1.4, NE)	18	0	18 (100)	NE (NE, NE)	NE (NE, NE) 0.9971	0.1483	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

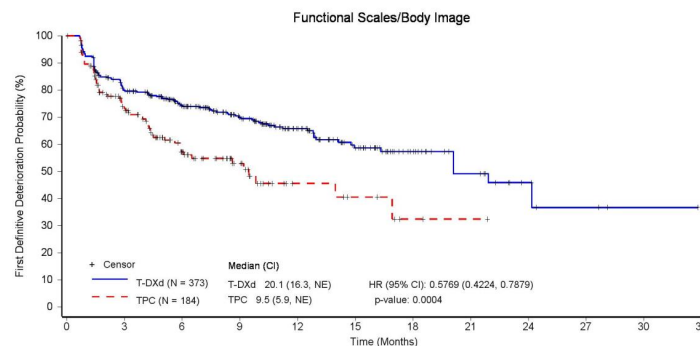
[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 15SEP2022 – 12:19; Program name: T3\_EQ5D\_FD\_2\_FAS.sas; Output name: T3\_EORTC BR45\_DD\_2\_FAS.rf

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Patients still at risk:

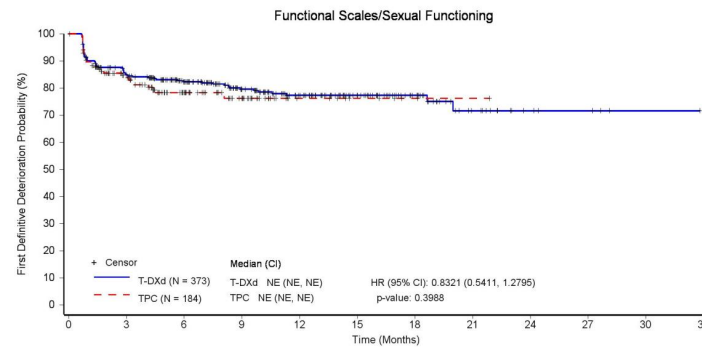
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T-DXd (N = 373)	373	257	196	146	93	56	32	18	6	3	1	0
TPC (N = 184)	184	97	51	26	9	6	2	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

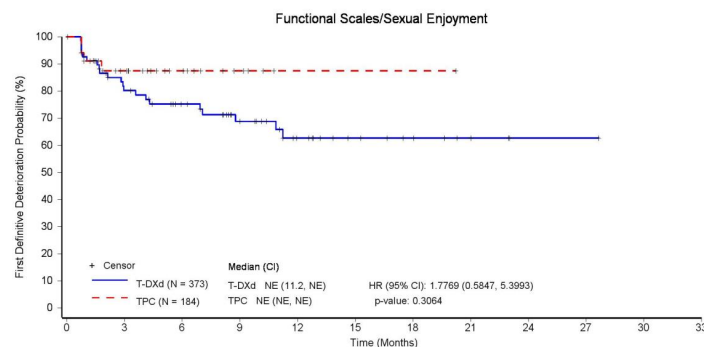
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	267	212	159	107	68	40	17	6	4	1	0
TPC (N = 184)	184	101	56	31	9	5	2	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

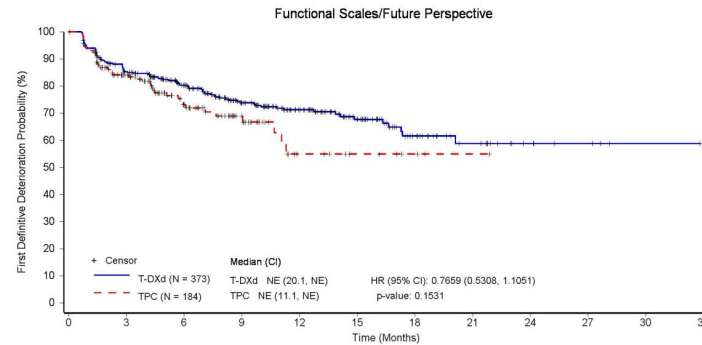
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	50	40	28	16	10	7	4	1	1	0	0
TPC (N = 184)	184	21	11	5	1	1	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

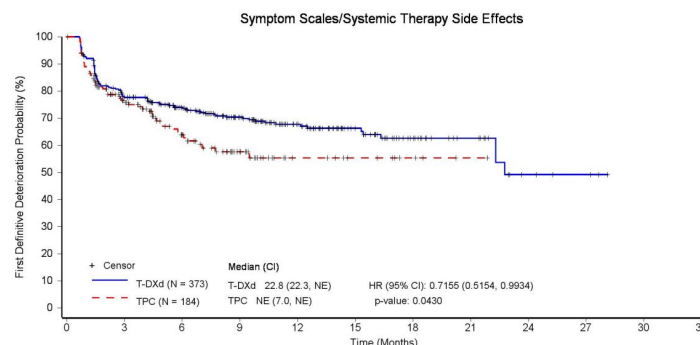
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	279	221	160	107	66	34	20	7	4	1	0
TPC (N = 184)	184	113	62	32	10	6	3	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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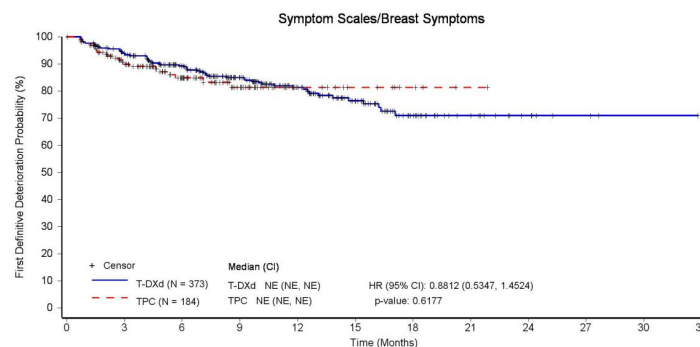
Patients still at risk:		3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	251	198	148	96	58	33	19	5	3	0	0
TPC (N = 184)	184	101	59	31	12	8	4	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	297	239	184	120	72	37	18	7	3	1	0
TPC (N = 184)	184	117	67	36	13	8	4	1	0	0	0	0

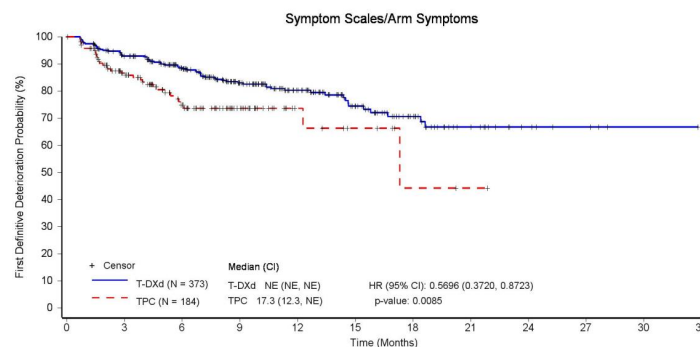
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

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Patients still at risk:

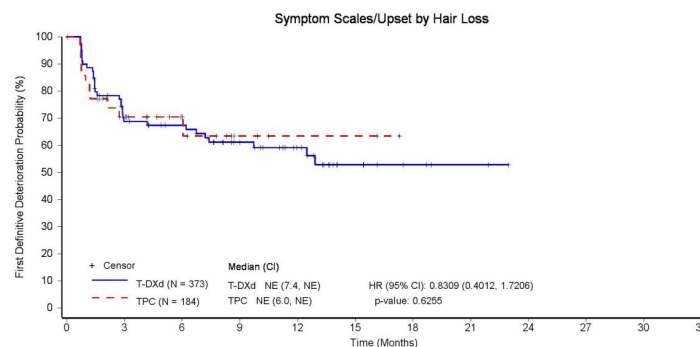
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	300	243	179	114	69	41	20	7	4	1	0
TPC (N = 184)	184	110	63	31	10	6	2	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

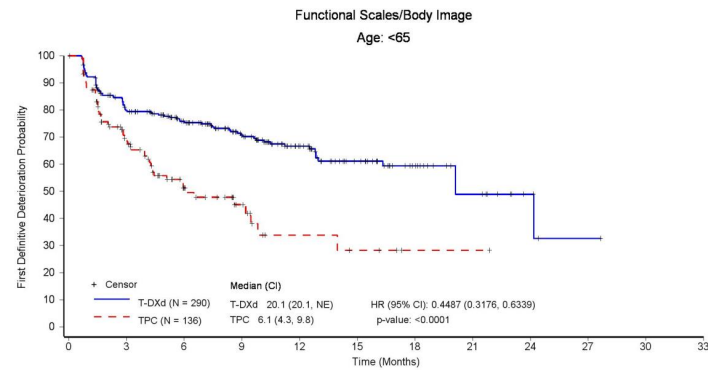
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	50	44	31	21	9	4	2	0	0	0	0
TPC (N = 184)	184	20	11	4	2	2	0	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 DE.F.3.10.4 - EORTC QLQ-BR45 - Definitive deterioration - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

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Patients still at risk:

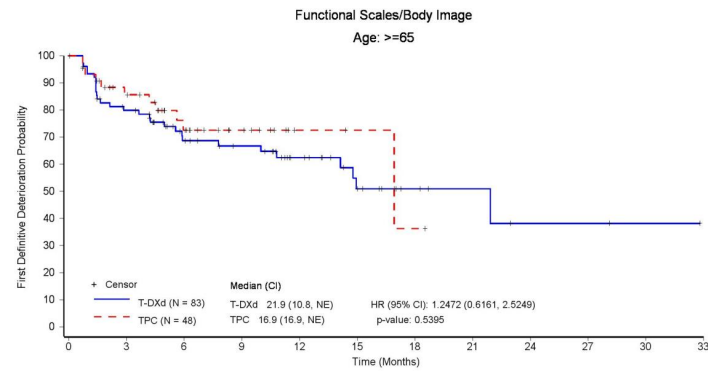
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 290)	290	200	157	113	71	43	26	14	4	1	0	0
TPC (N = 136)	136	65	31	15	6	4	1	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

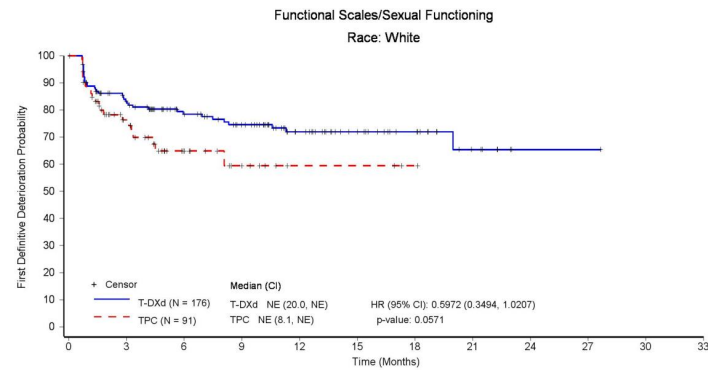
T-DXd (N = 83)	83	57	39	33	22	13	6	4	2	2	1	0
TPC (N = 48)	48	32	20	11	3	2	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

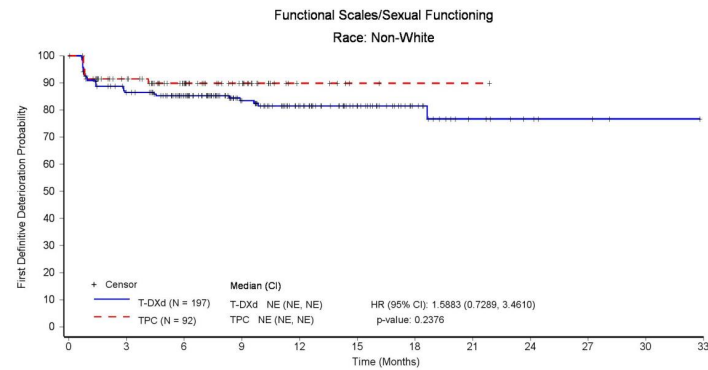
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 176)	176	114	86	72	46	30	20	8	1	1	0	0
TPC (N = 91)	91	37	17	9	3	3	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

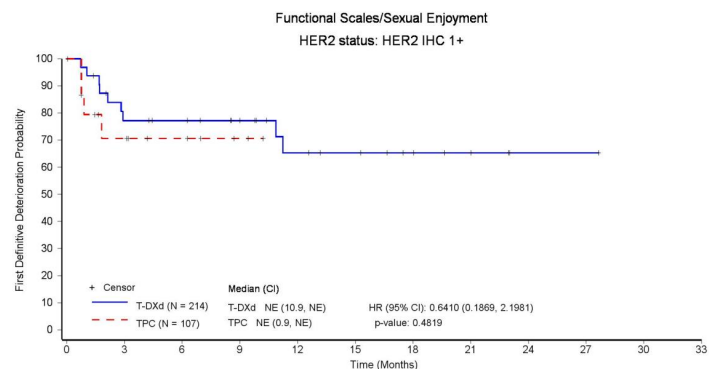
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 197)	197	153	126	87	61	38	20	9	5	3	1	0
TPC (N = 92)	92	63	39	22	6	2	1	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:21; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCQR45\_DD\_4\_FAS.rf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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Patients still at risk:

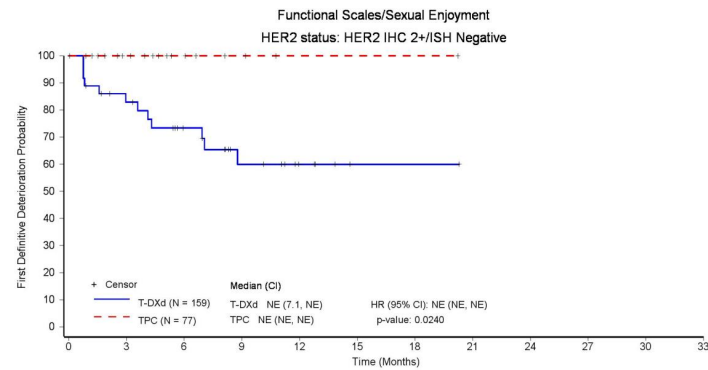
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 214)	214	23	21	17	11	9	6	4	1	1	0	0
TPC (N = 107)	107	8	5	2	0	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:21; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCQR45\_DD\_4\_FAS.rf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 159)	159	27	19	11	5	1	1	0	0	0	0	0
TPC (N = 77)	77	13	6	3	1	1	1	0	0	0	0	0

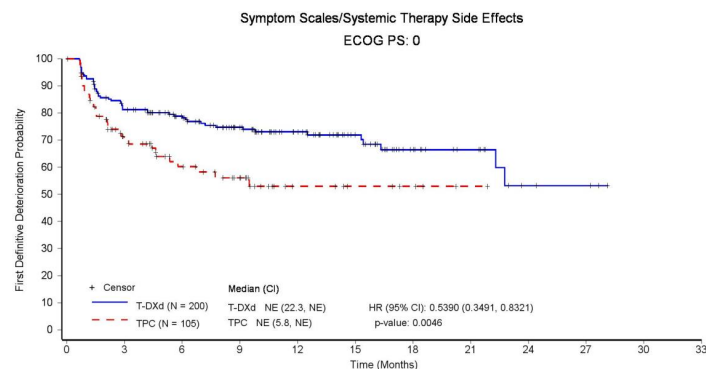
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:21; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCQR45\_DD\_4\_FAS.rf



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Patients still at risk:

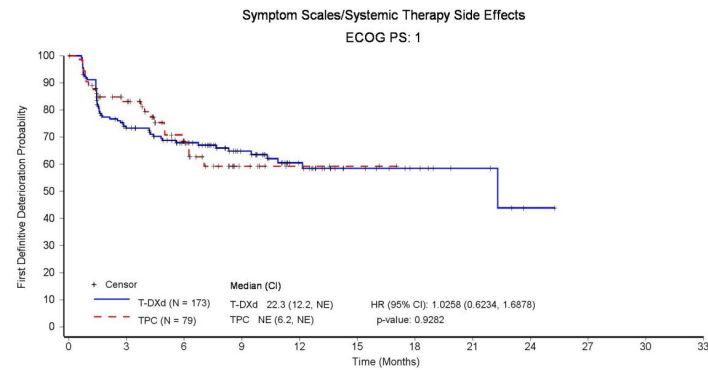
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 200)	200	147	120	96	66	42	23	14	4	3	0	0
TPC (N = 105)	105	51	33	23	9	6	4	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:21; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCQR45\_DD\_4\_FAS.rf

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Patients still at risk:

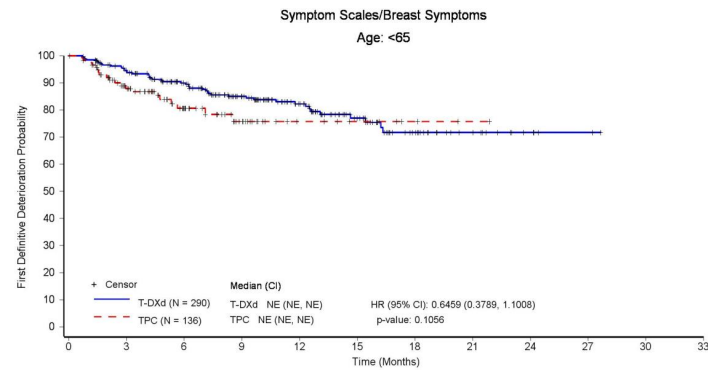
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 173)	173	104	78	52	30	16	10	5	1	0	0	0
TPC (N = 79)	79	50	26	8	3	2	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:21; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCQR45\_DD\_4\_FAS.rf

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Patients still at risk:

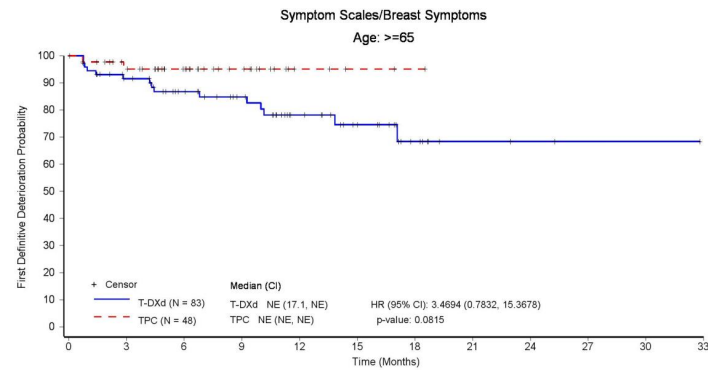
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 290)	290	237	191	145	94	54	29	15	5	2	0	0
TPC (N = 136)	136	81	43	22	9	6	3	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

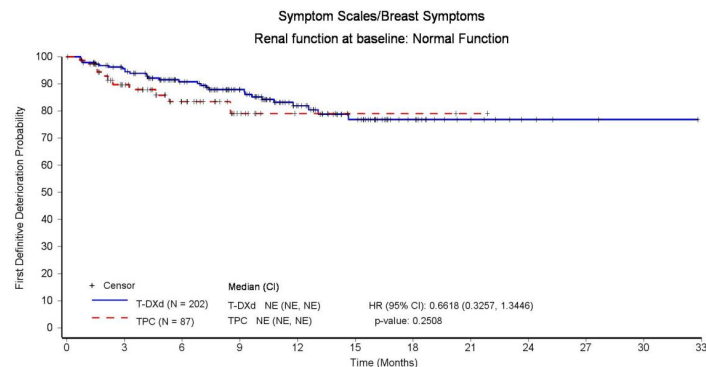
T-DXd (N = 83)	83	60	48	39	26	18	8	3	2	1	1	0
TPC (N = 48)	48	36	24	14	4	2	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:21; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCQR45\_DD\_4\_FAS.rf

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Patients still at risk:

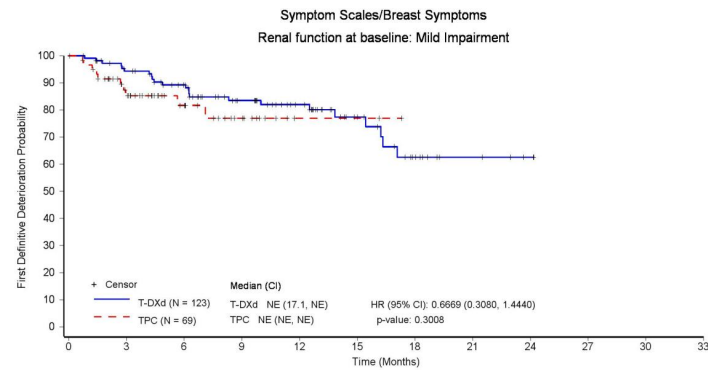
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 202)	202	167	130	101	60	39	20	10	4	2	1	0
TPC (N = 87)	87	52	29	13	6	2	2	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

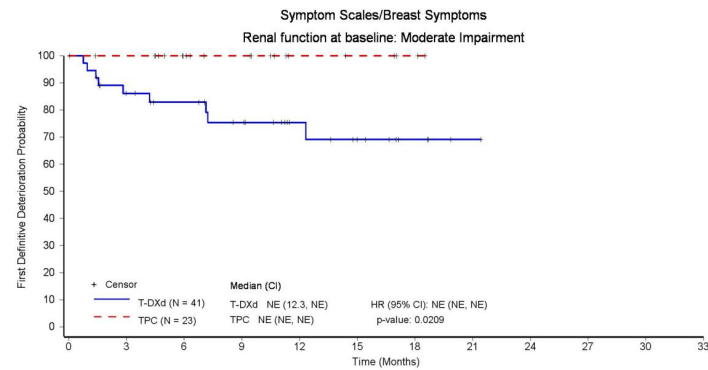
T-DXd (N = 123)	123	97	82	61	46	24	12	6	2	0	0	0
TPC (N = 69)	69	40	22	11	2	2	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:21; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCQR45\_DD\_4\_FAS.rf

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Patients still at risk:

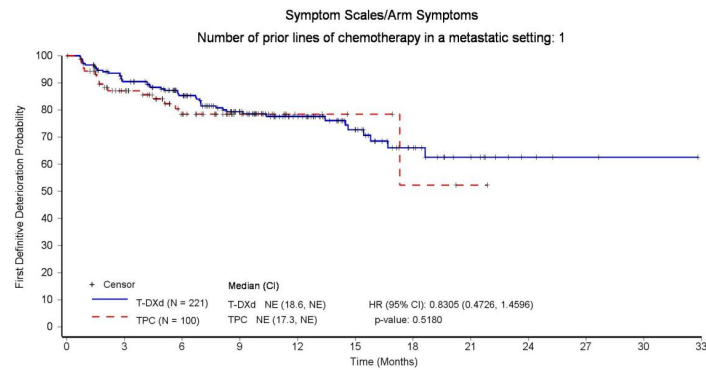
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T-DXd (N = 41)	41	28	24	19	12	8	4	1	0	0	0	0
TPC (N = 23)	23	21	14	11	5	4	2	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:21; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F3\_EORTCQR45\_DD\_4\_FAS.rf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 221)	221	174	139	103	70	41	22	12	4	2	1	0
TPC (N = 100)	100	65	37	18	6	4	2	1	0	0	0	0

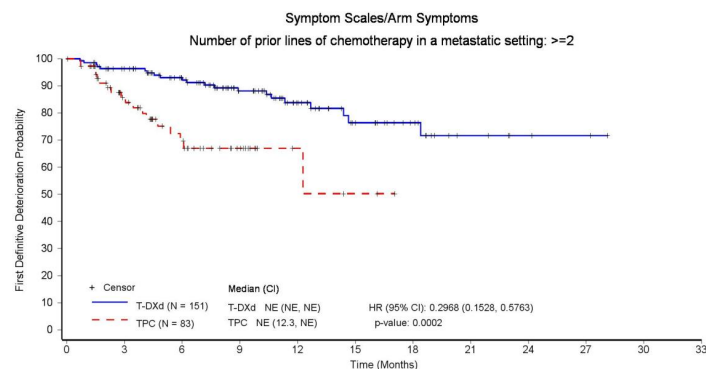
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 Data Intelligence – Evidence Generation  
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 Statistical analyses for AMNOG (HTA Germany)  
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Patients still at risk:

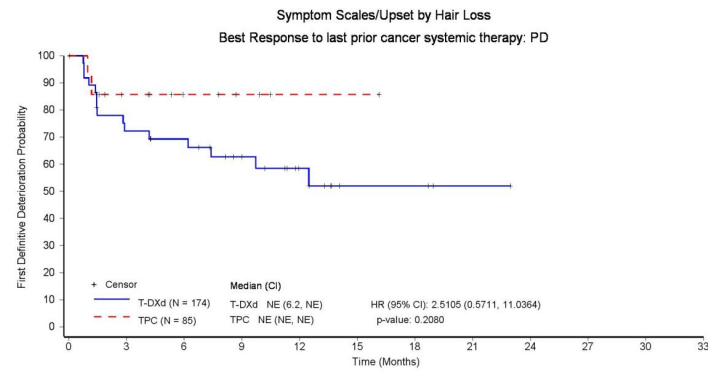
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 151)	151	125	103	75	43	27	18	7	3	2	0	0
TPC (N = 83)	83	45	26	13	4	2	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

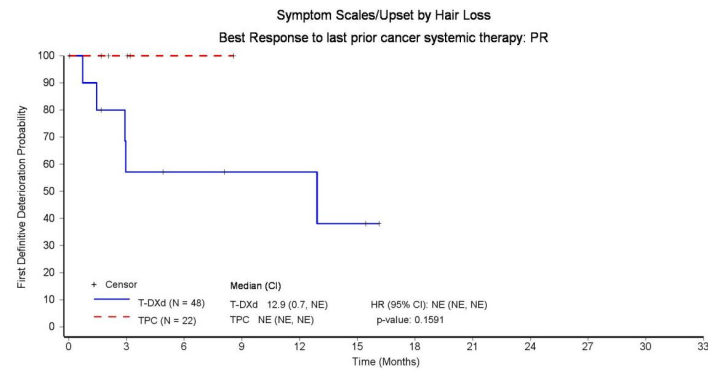
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 174)	174	25	22	16	9	3	3	1	0	0	0	0
TPC (N = 85)	85	9	5	3	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

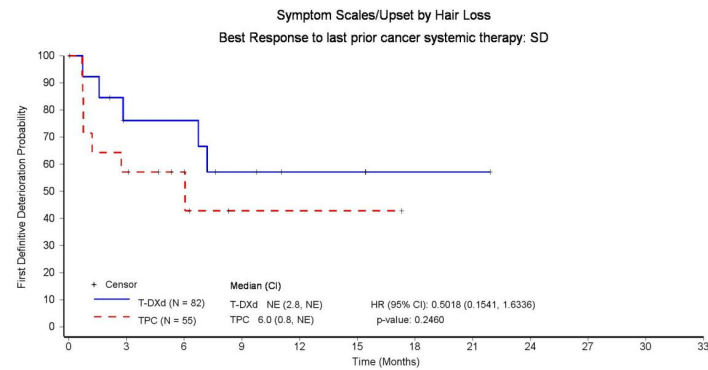
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 48)	48	5	4	3	3	2	0	0	0	0	0	0
TPC (N = 22)	22	3	1	0	0	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 82)	82	8	8	5	3	3	1	1	0	0	0	0
TPC (N = 55)	55	8	5	1	1	1	0	0	0	0	0	0

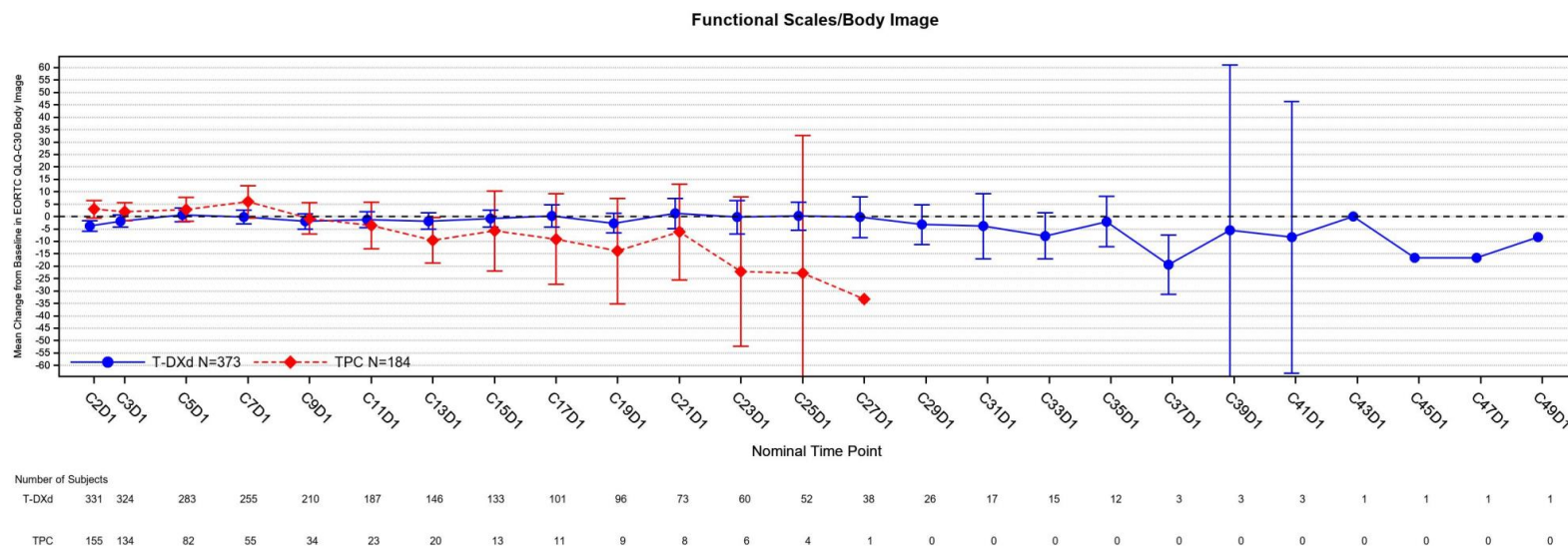
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DE.F.3.11.1 - EORTC QLQ-BR45 - Mean change from baseline plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



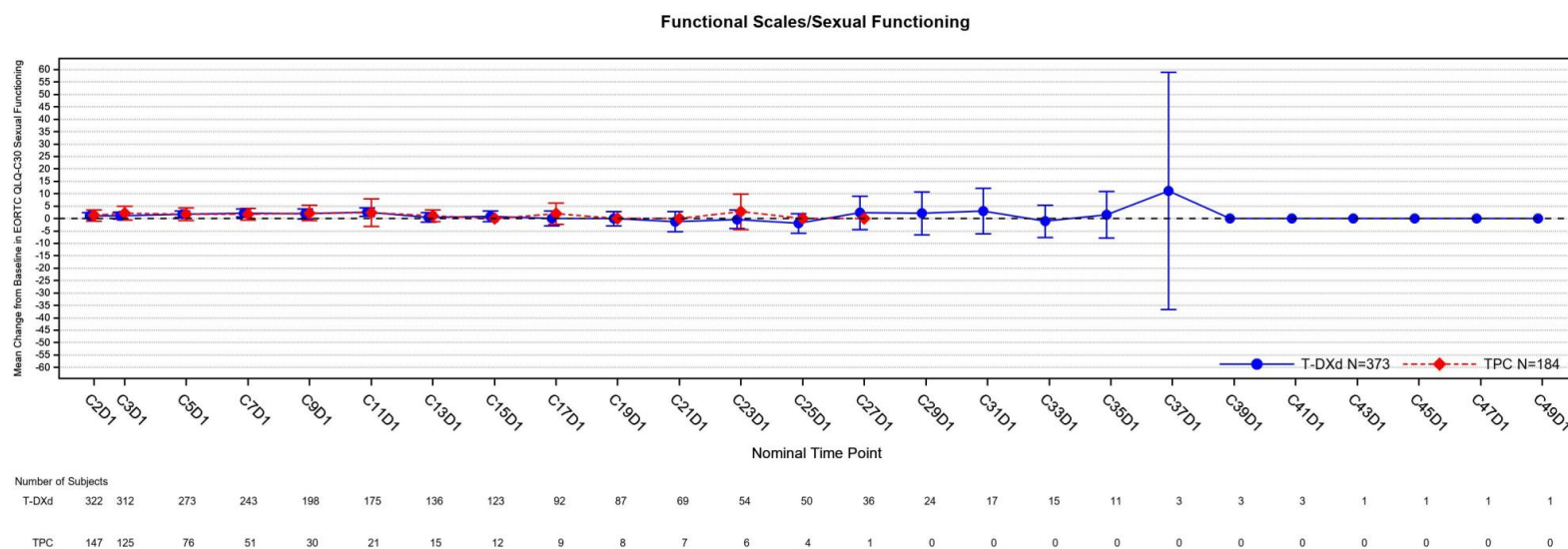
Number of subjects is number of subjects with an observation at the visit (i.e. scale score calculable for the visit). Error bars represent the 95% confidence interval for the mean value. A high score for EORTC-QLQ-C30 global health status represents a low/unhealthy level of functioning; a high score for a EORTC-QLQ-C30 and EORTC-QLQ-BR45 symptom scale/item represents a high level of symptomology/problems; a high score for a EORTC-QLQ-C30 and EORTC-QLQ-BR45 functional scale represents a low/unhealthy level of functioning A high score for the EQ-5D-5L VAS represents a low/unhealthy level of functioning;

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.3.11.1 - EORTC QLQ-BR45 - Mean change from baseline plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



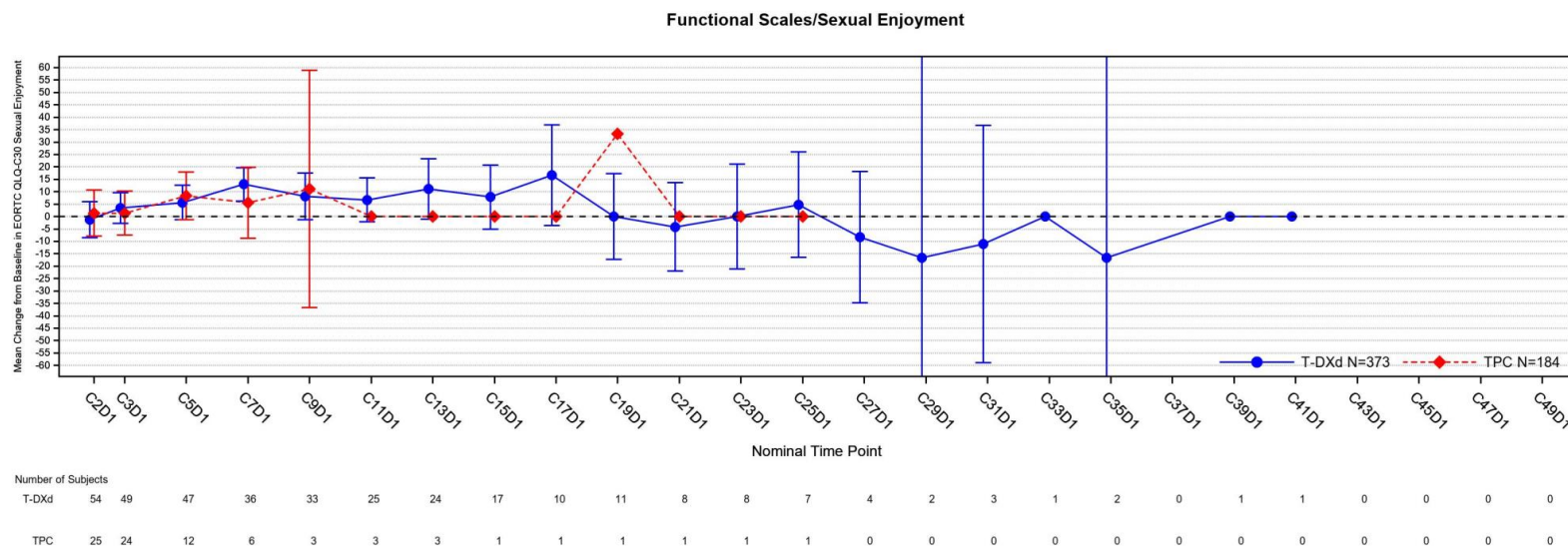
Number of subjects is number of subjects with an observation at the visit (i.e. scale score calculable for the visit). Error bars represent the 95% confidence interval for the mean value. A high score for EORTC-QLQ-C30 global health status represents a low/unhealthy level of functioning; a high score for a EORTC-QLQ-C30 and EORTC-QLQ-BR45 symptom scale/item represents a high level of symptomology/problems; a high score for a EORTC-QLQ-C30 and EORTC-QLQ-BR45 functional scale represents a low/unhealthy level of functioning A high score for the EQ-5D-5L VAS represents a low/unhealthy level of functioning;

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.3.11.1 - EORTC QLQ-BR45 - Mean change from baseline plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



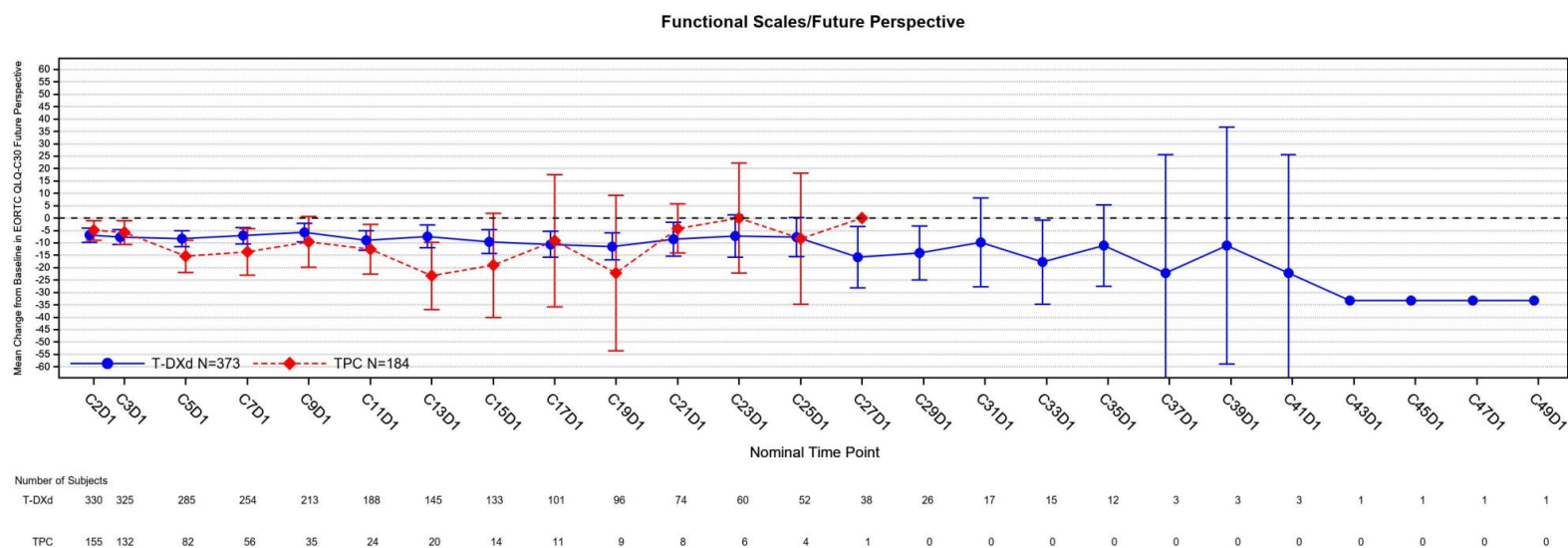
Number of subjects is number of subjects with an observation at the visit (i.e. scale score calculable for the visit). Error bars represent the 95% confidence interval for the mean value. A high score for EORTC-QLQ-C30 global health status represents a low/unhealthy level of functioning; a high score for a EORTC-QLQ-C30 and EORTC-QLQ-BR45 symptom scale/item represents a high level of symptomology/problems; a high score for a EORTC-QLQ-C30 and EORTC-QLQ-BR45 functional scale represents a low/unhealthy level of functioning A high score for the EQ-5D-5L VAS represents a low/unhealthy level of functioning;

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Number of subjects is number of subjects with an observation at the visit (i.e. scale score calculable for the visit). Error bars represent the 95% confidence interval for the mean value. A high score for EORTC-QLQ-C30 global health status represents a low/unhealthy level of functioning; a high score for a EORTC-QLQ-C30 and EORTC-QLQ-BR45 symptom scale/item represents a high level of symptomology/problems; a high score for a EORTC-QLQ-C30 and EORTC-QLQ-BR45 functional scale represents a low/unhealthy level of functioning A high score for the EQ-5D-5L VAS represents a low/unhealthy level of functioning;

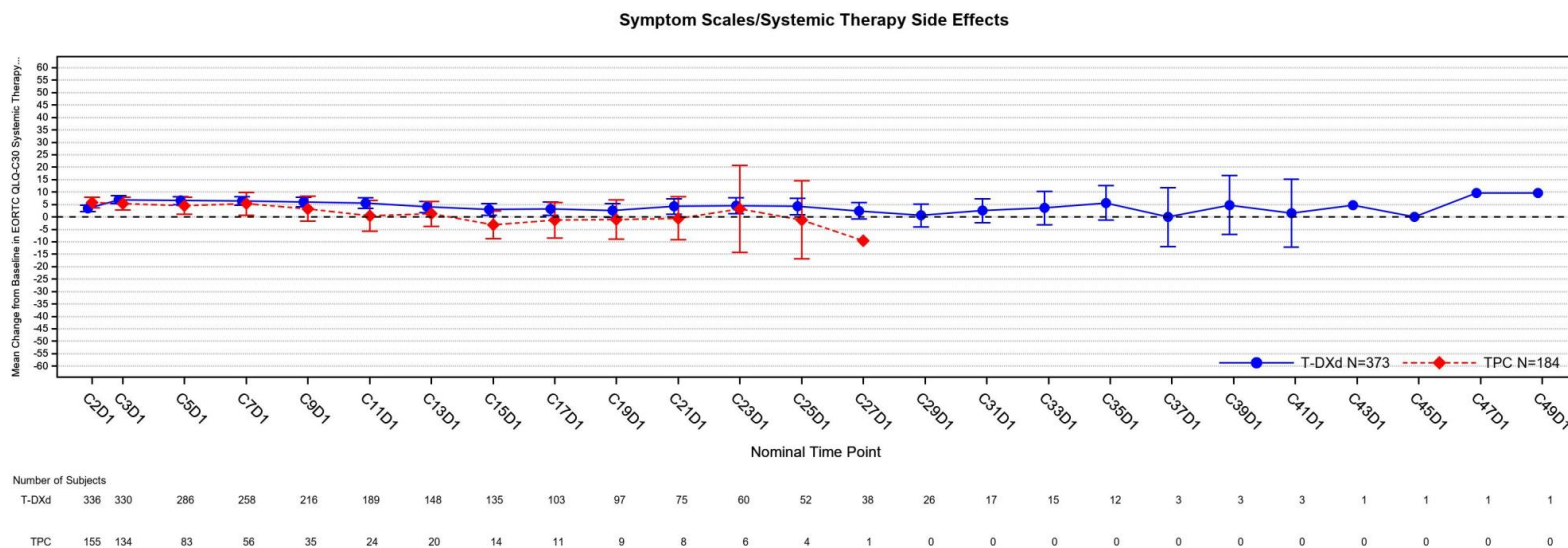
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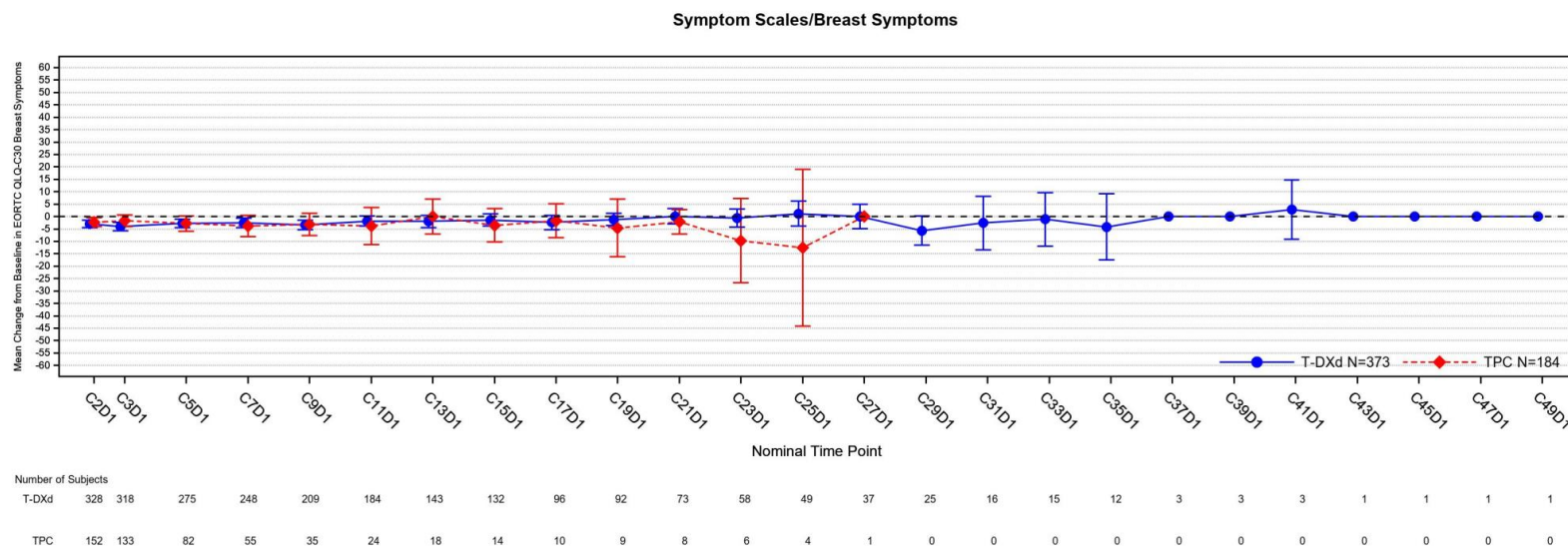
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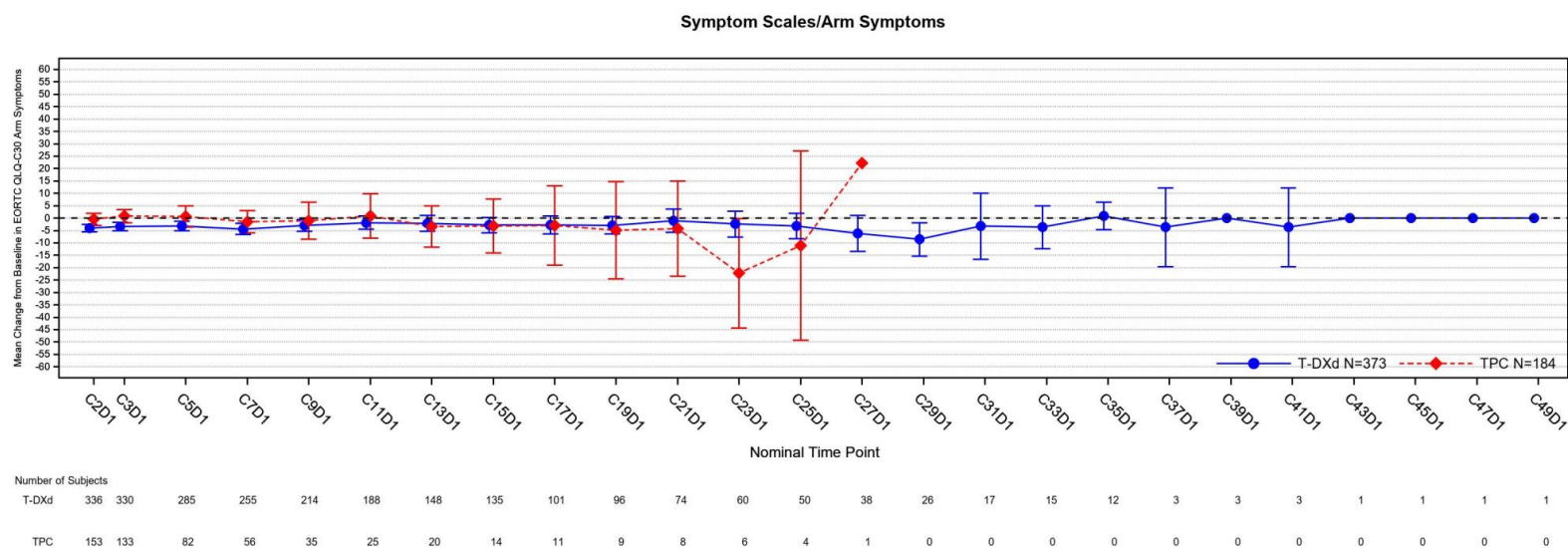
Number of subjects is number of subjects with an observation at the visit (i.e. scale score calculable for the visit). Error bars represent the 95% confidence interval for the mean value. A high score for EORTC-QLQ-C30 global health status represents a low/unhealthy level of functioning; a high score for a EORTC-QLQ-C30 and EORTC-QLQ-BR45 symptom scale/item represents a high level of symptomology/problems; a high score for a EORTC-QLQ-C30 and EORTC-QLQ-BR45 functional scale represents a low/unhealthy level of functioning A high score for the EQ-5D-5L VAS represents a low/unhealthy level of functioning;

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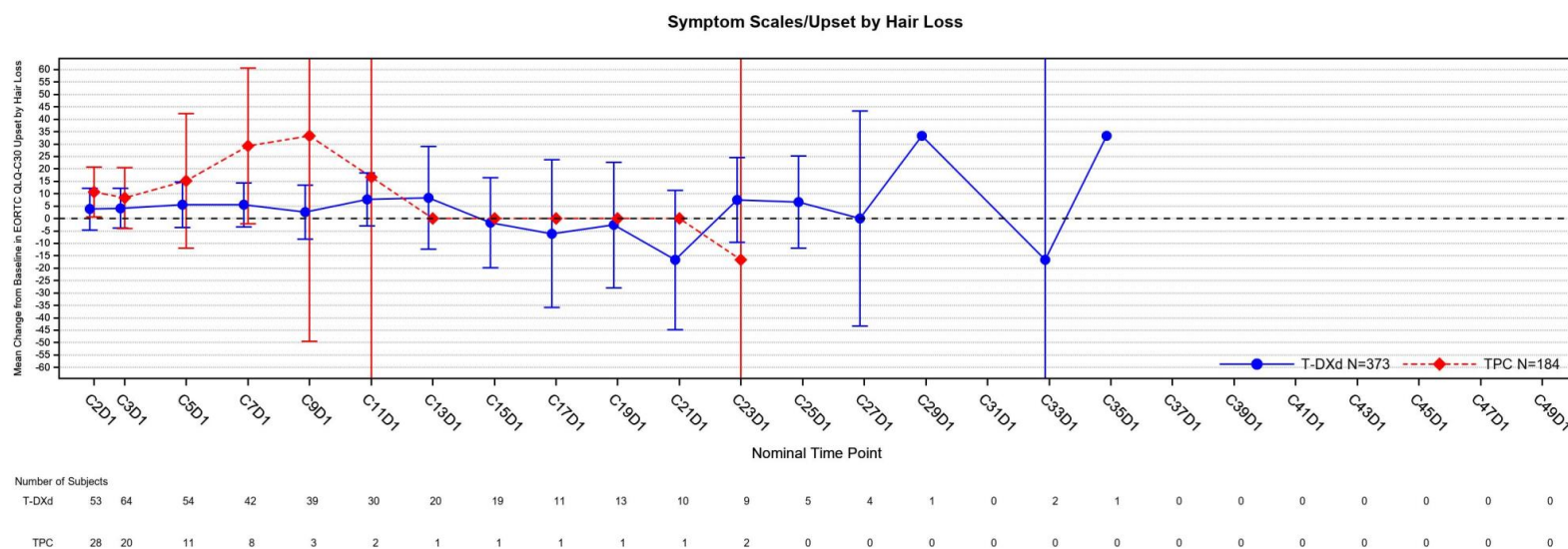
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Functional Scales/Body Image\*

Parameter	n[a]	Estimate [b]	Standard Error	P-value
Intercept		2.06	3.042	0.4986
Treatment				
T-DXd	347	-5.09	1.931	0.0086
TPC	164	0		
Time of Visit		0.00	0.005	0.7668
Treatment*Time of Visit		0.00	0.005	0.9235

A negative estimate denotes an improvement in health status in terms of the scale/item being evaluated.

[a] n is the number of subjects included in the model in each treatment group.

[b] Estimates obtained from a mixed model including terms for treatment, the randomization stratification factors, time of visit (days), and treatment-by-time of visit interaction as well as the intercept as random effect.

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Functional Scales/Sexual Functioning\*

Parameter	n[a]	Estimate [b]	Standard Error	P-value
Intercept		2.67	1.784	0.1343
Treatment				
T-DXd	342	-0.97	1.142	0.3983
TPC	156	0		
Time of Visit		0.00	0.003	0.4464
Treatment*Time of Visit		0.00	0.003	0.8742

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Functional Scales/Sexual Enjoyment\*

Parameter	n[a]	Estimate [b]	Standard Error	P-value
Intercept		13.19	8.105	0.1069
Treatment				
T-DXd	68	3.60	4.758	0.4509
TPC	34	0		
Time of Visit		0.02	0.016	0.3366
Treatment*Time of Visit		0.00	0.017	0.7880

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Functional Scales/Future Perspective\*

Parameter	n[a]	Estimate [b]	Standard Error	P-value
Intercept		-3.07	3.731	0.4102
Treatment				
T-DXd	348	-0.74	2.392	0.7557
TPC	163	0		
Time of Visit		0.01	0.007	0.3616
Treatment*Time of Visit		-0.01	0.007	0.1680

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Symptom Scales/Systemic Therapy Side Effects\*

Parameter	n[a]	Estimate [b]	Standard Error	P-value
Intercept		3.36	1.870	0.0729
Treatment				
T-DXd	350	0.18	1.194	0.8825
TPC	164	0		
Time of Visit		0.00	0.003	0.9366
Treatment*Time of Visit		0.00	0.003	0.1704

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Symptom Scales/Breast Symptoms\*

Parameter	n[a]	Estimate [b]	Standard Error	P-value
Intercept		-7.80	2.046	0.0002
Treatment				
T-DXd	343	-1.42	1.287	0.2687
TPC	163	0		
Time of Visit		0.00	0.003	0.8854
Treatment*Time of Visit		0.00	0.003	0.4469

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Symptom Scales/Arm Symptoms\*

Parameter	n[a]	Estimate [b]	Standard Error	P-value
Intercept		-4.32	2.399	0.0723
Treatment				
T-DXd	350	-4.64	1.523	0.0024
TPC	163	0		
Time of Visit		-0.01	0.004	0.0419
Treatment*Time of Visit		0.01	0.004	0.0168

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Symptom Scales/Upset by Hair Loss\*

Parameter	n[a]	Estimate [b]	Standard Error	P-value
Intercept		-3.79	10.502	0.7186
Treatment				
T-DXd	79	-3.21	6.089	0.5983
TPC	35	0		
Time of Visit		-0.02	0.023	0.4148
Treatment*Time of Visit		0.00	0.024	0.8968

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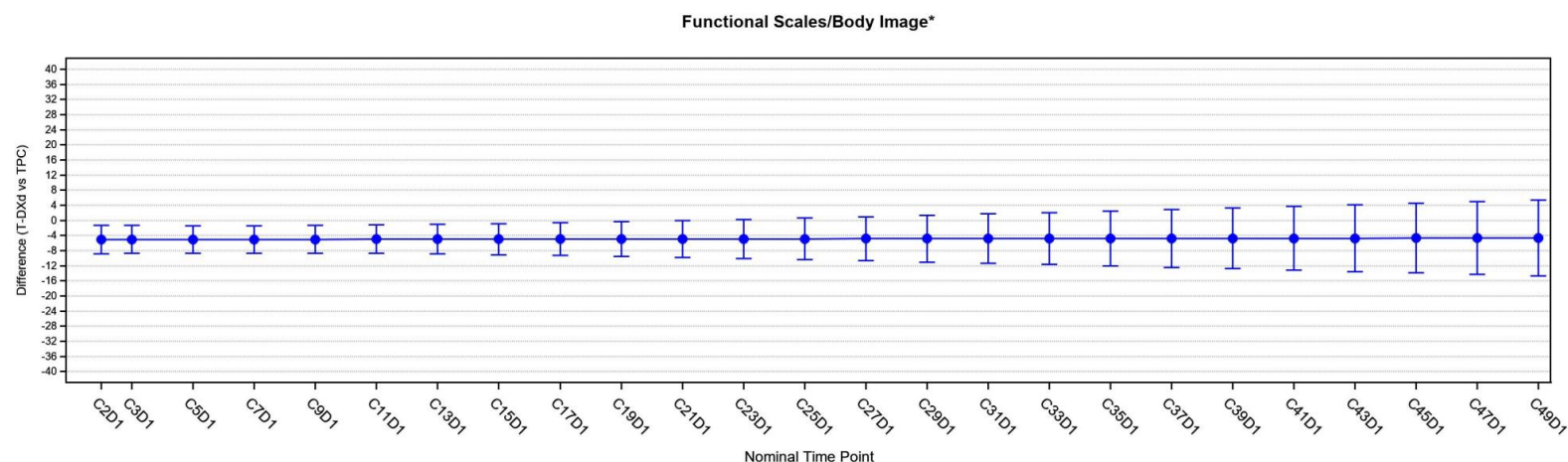
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DE.F.3.12.2 - EORTC QLQ-BR45 - Plot of least-square means of repeated measures analysis of change from baseline - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Least square mean (LSM) estimates of trastuzumab deruxtecan versus comparator and their 95% CI are calculated using a restricted maximum likelihood (REML) based mixed model including terms for treatment, the randomization stratification factors, time of visit (days), and treatment by time of visit interaction as well as the intercept as random effect. A high score for global health status represents a low quality of life (change of direction from raw score); a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomology/problems.

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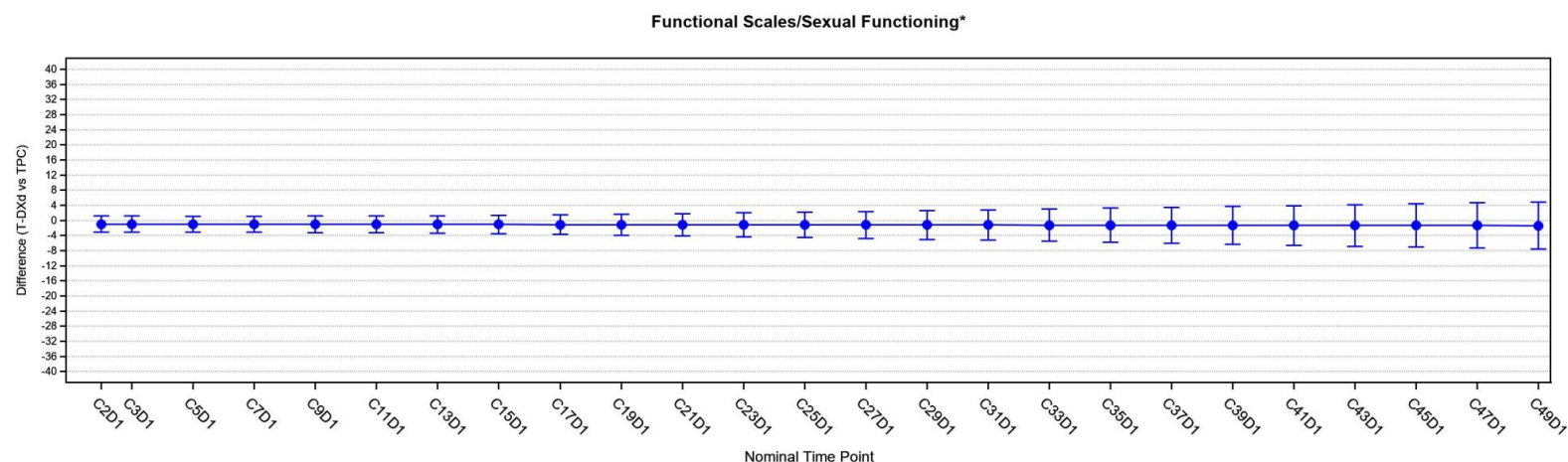
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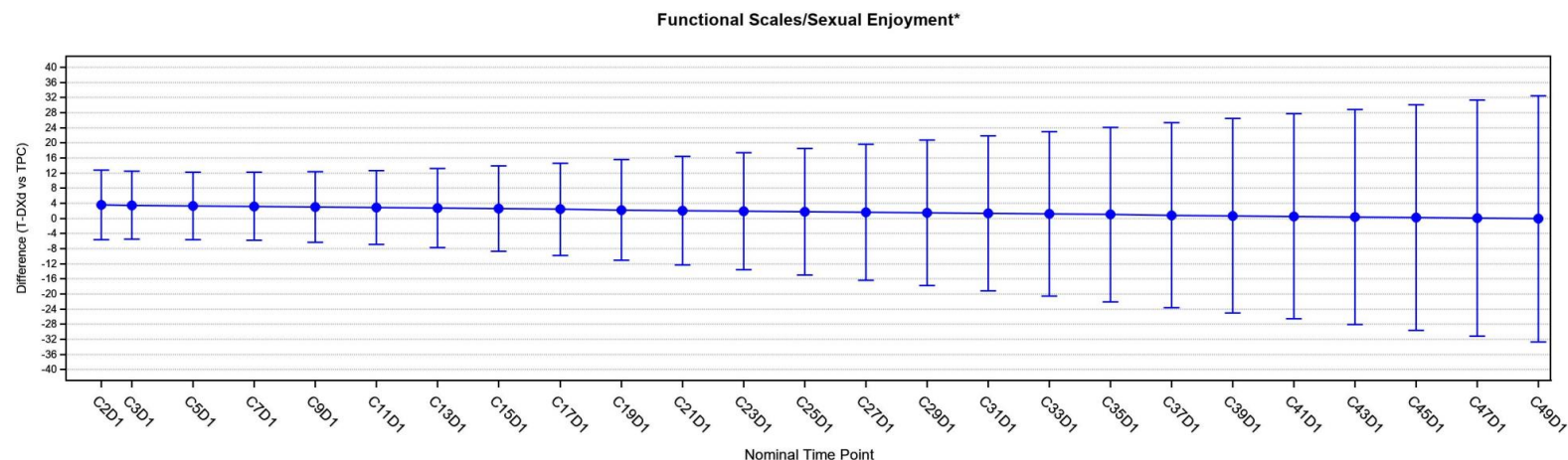
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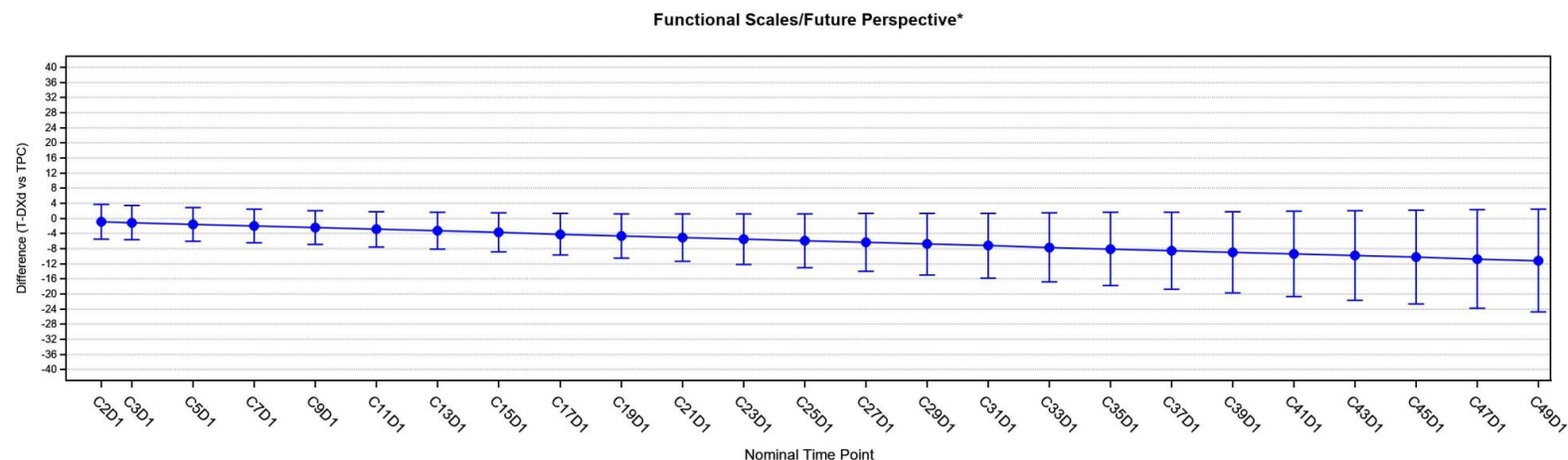
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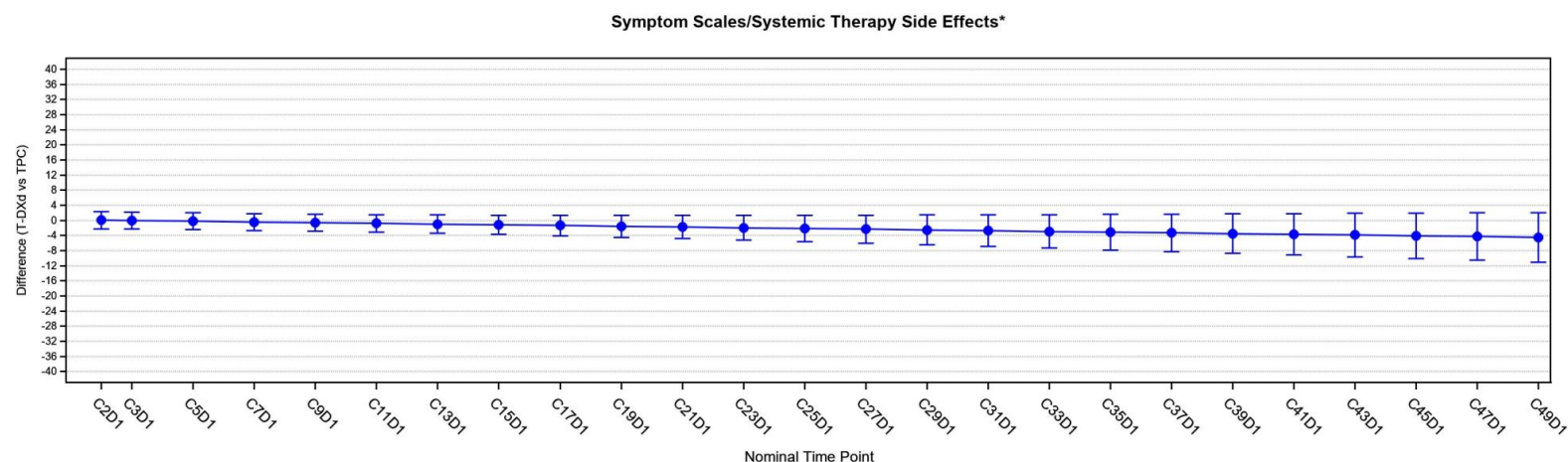
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DE.F.3.12.2 - EORTC QLQ-BR45 - Plot of least-square means of repeated measures analysis of change from baseline - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Least square mean (LSM) estimates of trastuzumab deruxtecan versus comparator and their 95% CI are calculated using a restricted maximum likelihood (REML) based mixed model including terms for treatment, the randomization stratification factors, time of visit (days), and treatment by time of visit interaction as well as the intercept as random effect. A high score for global health status represents a low quality of life (change of direction from raw score); a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomology/problems.

\* Unstructured covariance matrix was used to model the correlation within subject. † AR(1) covariance structure used to model correlation within subjects. ‡ Compound symmetry covariance structure used to model correlation within subjects

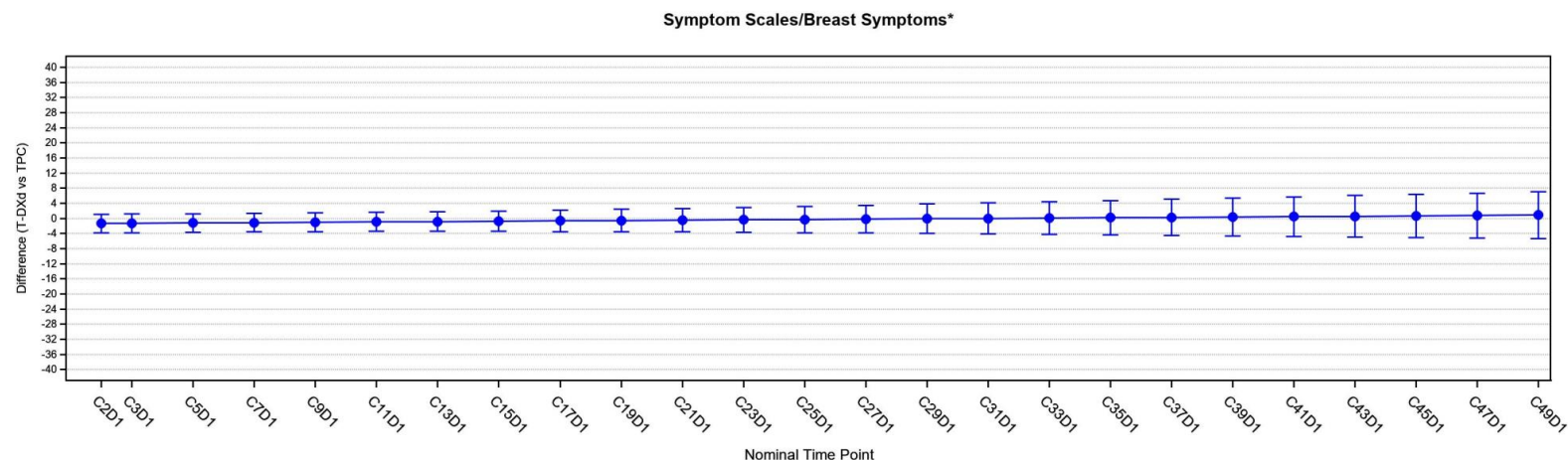
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Run date: 15SEP2022 – 12:23; Program name: F3\_EQ5D\_MMRM\_2\_FAS.sas; Output name: F3\_EORTC BR45\_MMRM\_2\_FAS.rtf

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Least square mean (LSM) estimates of trastuzumab deruxtecan versus comparator and their 95% CI are calculated using a restricted maximum likelihood (REML) based mixed model including terms for treatment, the randomization stratification factors, time of visit (days), and treatment by time of visit interaction as well as the intercept as random effect. A high score for global health status represents a low quality of life (change of direction from raw score); a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomology/problems.

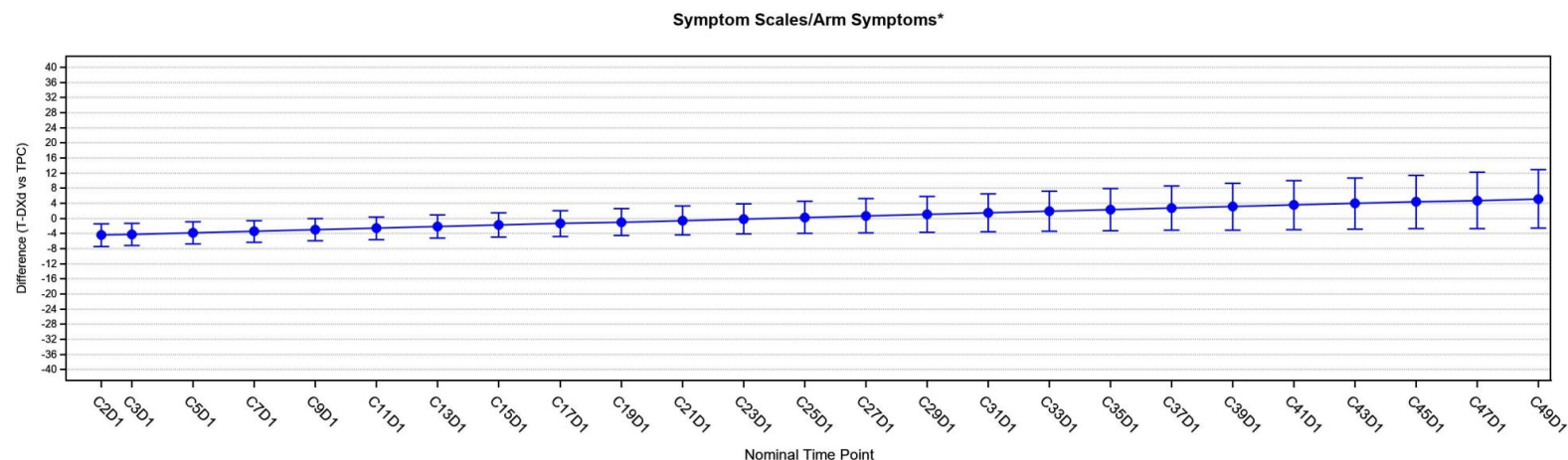
\* Unstructured covariance matrix was used to model the correlation within subject. † AR(1) covariance structure used to model correlation within subjects. ‡ Compound symmetry covariance structure used to model correlation within subjects

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 15SEP2022 – 12:23; Program name: F3\_EQ5D\_MMRM\_2\_FAS.sas; Output name: F3\_EORTCBR45\_MMRM\_2\_FAS.rtf

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Least square mean (LSM) estimates of trastuzumab deruxtecan versus comparator and their 95% CI are calculated using a restricted maximum likelihood (REML) based mixed model including terms for treatment, the randomization stratification factors, time of visit (days), and treatment by time of visit interaction as well as the intercept as random effect. A high score for global health status represents a low quality of life (change of direction from raw score); a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomology/problems.

\* Unstructured covariance matrix was used to model the correlation within subject. † AR(1) covariance structure used to model correlation within subjects. ‡ Compound symmetry covariance structure used to model correlation within subjects

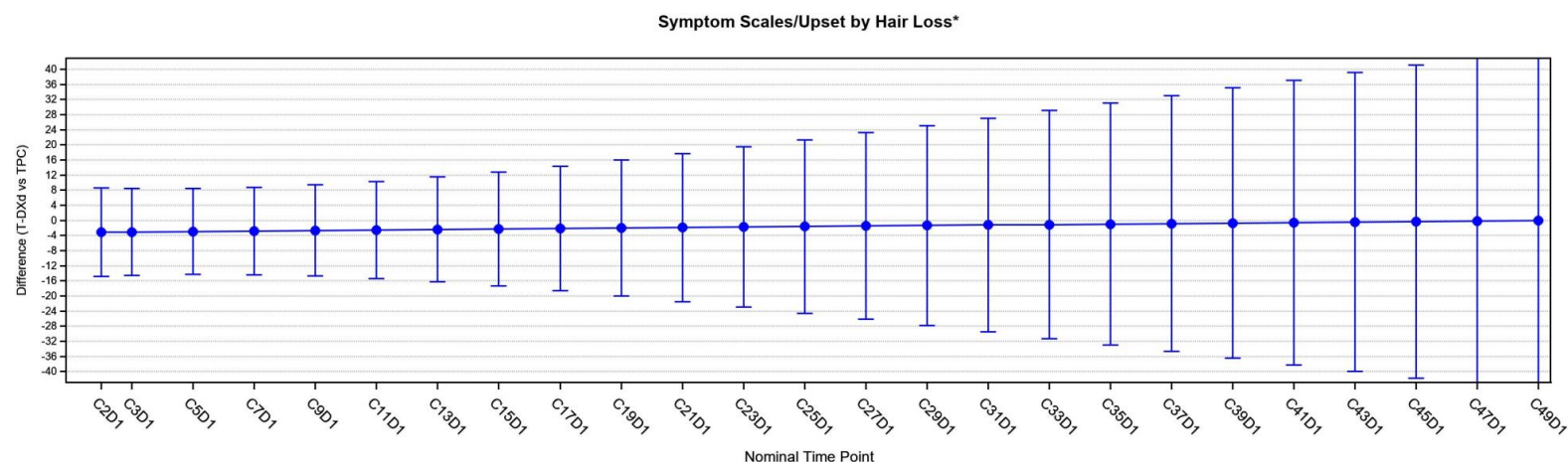
Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 15SEP2022 – 12:23; Program name: F3\_EQ5D\_MMRM\_2\_FAS.sas; Output name: F3\_EORTC BR45\_MMRM\_2\_FAS.rtf

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Least square mean (LSM) estimates of trastuzumab deruxtecan versus comparator and their 95% CI are calculated using a restricted maximum likelihood (REML) based mixed model including terms for treatment, the randomization stratification factors, time of visit (days), and treatment by time of visit interaction as well as the intercept as random effect. A high score for global health status represents a low quality of life (change of direction from raw score); a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomology/problems.

\* Unstructured covariance matrix was used to model the correlation within subject. † AR(1) covariance structure used to model correlation within subjects. ‡ Compound symmetry covariance structure used to model correlation within subjects

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 15SEP2022 – 12:23; Program name: F3\_EQ5D\_MMRM\_2\_FAS.sas; Output name: F3\_EORTCBR45\_MMRM\_2\_FAS.rf

**Anhang 4-G 3.5: EORTC QLQ-BR45 (MID 10 Punkte)**

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Functional Scales/Body Image

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	152 (40.8)	84 (45.7)	
Number of subjects censored, n (%)	221 (59.2)	100 (54.3)	
Median time to first event (months) [a]	13.8	5.1	
95% Confidence Interval	[9.7, NE]	[3.0, 9.8]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.6395
95% Confidence Interval			[0.4870, 0.8397]
p-value			0.0013
Stratified log-rank p-value [c]			0.0012

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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 Run date: 10JAN2023 – 19:33; Program name: T3\_EQ5D\_FD\_1\_FAS.sas; Output name: T28BR45.rtf

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#### Functional Scales/Sexual Functioning

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	78 (20.9)	34 (18.5)	
Number of subjects censored, n (%)	295 (79.1)	150 (81.5)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.9025
95% Confidence Interval			[0.6004, 1.3566]
p-value			0.6217
Stratified log-rank p-value [c]			0.6117

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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#### Functional Scales/Sexual Enjoyment

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	33 (8.8)	8 (4.3)	
Number of subjects censored, n (%)	340 (91.2)	176 (95.7)	
Median time to first event (months) [a]	11.2	12.0	
95% Confidence Interval	[4.3, NE]	[NE, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			2.1284
95% Confidence Interval			[0.8626, 5.2516]
p-value			0.1012
Stratified log-rank p-value [c]			0.0943

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Functional Scales/Future Perspective

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	131 (35.1)	58 (31.5)	
Number of subjects censored, n (%)	242 (64.9)	126 (68.5)	
Median time to first event (months) [a]	17.3	NE	
95% Confidence Interval	[14.9, NE]	[7.7, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.8821
95% Confidence Interval			[0.6433, 1.2095]
p-value			0.4360
Stratified log-rank p-value [c]			0.4392

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Symptom Scales/Systemic Therapy Side Effects

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	211 (56.6)	101 (54.9)	
Number of subjects censored, n (%)	162 (43.4)	83 (45.1)	
Median time to first event (months) [a]	4.2	3.1	
95% Confidence Interval	[2.8, 5.9]	[1.6, 4.7]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.8255
95% Confidence Interval			[0.6487, 1.0505]
p-value			0.1189
Stratified log-rank p-value [c]			0.1166

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Symptom Scales/Breast Symptoms

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	99 (26.5)	38 (20.7)	
Number of subjects censored, n (%)	274 (73.5)	146 (79.3)	
Median time to first event (months) [a] 95% Confidence Interval	NE [20.3, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.9457 [0.6451, 1.3862] 0.7746
Stratified log-rank p-value [c]			0.7804

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Symptom Scales/Arm Symptoms

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	179 (48.0)	81 (44.0)	
Number of subjects censored, n (%)	194 (52.0)	103 (56.0)	
Median time to first event (months) [a]	8.3	5.1	
95% Confidence Interval	[7.0, 11.2]	[3.1, 7.0]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.7390
95% Confidence Interval			[0.5649, 0.9668]
p-value			0.0274
Stratified log-rank p-value [c]			0.0271

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:33; Program name: T3\_EQ5D\_FD\_1\_FAS.sas; Output name: T28BR45.rtf

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Symptom Scales/Upset by Hair Loss

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	42 (11.3)	16 (8.7)	
Number of subjects censored, n (%)	331 (88.7)	168 (91.3)	
Median time to first event (months) [a]	7.4	NE	
95% Confidence Interval	[2.9, NE]	[1.2, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.8114
95% Confidence Interval			[0.4293, 1.5336]
p-value			0.5199
Stratified log-rank p-value [c]			0.5325

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.5725
HER2 IHC 1+	214	88 (41.1)	126 (58.9)	13.9 (8.3, NE)	107	47 (43.9)	60 (56.1)	5.9 (2.8, 16.9)	0.6704 (0.4685, 0.9594)	0.0282
HER2 IHC 2+/ISH Negative	159	64 (40.3)	95 (59.7)	13.8 (7.5, NE)	77	37 (48.1)	40 (51.9)	4.2 (2.0, NE)	0.5693 (0.3778, 0.8579)	0.0065

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 10JAN2023 – 19:34; Program name: T3\_EQ5D\_FD\_2\_FAS.sas; Output name: T29BR45.rtf

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## Functional Scales/Body Image

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.1756
1	221	99 (44.8)	122 (55.2)	10.6 (6.3, 20.1)	100	48 (48.0)	52 (52.0)	5.4 (2.8, 16.9)	0.7338 (0.5184, 1.0387) 0.0809	0.0807
>=2	151	53 (35.1)	98 (64.9)	NE (10.5, NE)	83	36 (43.4)	47 (56.6)	4.4 (2.0, NE)	0.5044 (0.3279, 0.7759) 0.0018	0.0016

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Prior CDK4/6										0.8232
Yes	235	92 (39.1)	143 (60.9)	20.1 (8.3, NE)	118	50 (42.4)	68 (57.6)	5.1 (2.9, NE)	0.6770 (0.4785, 0.9580)	0.0265
No	98	46 (46.9)	52 (53.1)	12.5 (7.5, NE)	48	26 (54.2)	22 (45.8)	4.3 (2.1, 9.8)	0.5880 (0.3610, 0.9577)	0.0314

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											0.0128
<65	290	115 (39.7)	175 (60.3)	13.9 (9.7, NE)	136	68 (50.0)	68 (50.0)	4.2 (2.0, 6.1)	0.5122 (0.3778, 0.6945) <0.0001	<0.0001	
>=65	83	37 (44.6)	46 (55.4)	10.8 (4.2, NE)	48	16 (33.3)	32 (66.7)	16.9 (4.2, NE)	1.1733 (0.6507, 2.1157) 0.5952	0.5887	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5963
<75	359	149 (41.5)	210 (58.5)	12.8 (8.9, NE)	175	80 (45.7)	95 (54.3)	4.5 (2.9, 8.6)	0.6303 (0.4787, 0.8300) 0.0010	0.0009	
>=75	14	3 (21.4)	11 (78.6)	NE (7.0, NE)	9	4 (44.4)	5 (55.6)	16.9 (0.7, NE)	0.4745 (0.1053, 2.1372) 0.3316	0.3208	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.1929
White	176	60 (34.1)	116 (65.9)	NE (10.8, NE)	91	40 (44.0)	51 (56.0)	5.1 (2.8, NE)	0.5356 (0.3570, 0.8034) 0.0025	0.0023	
Non-White	197	92 (46.7)	105 (53.3)	9.7 (7.0, 20.1)	92	43 (46.7)	49 (53.3)	5.9 (2.1, 9.8)	0.7313 (0.5078, 1.0534) 0.0929	0.0923	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.5549
Asia	147	76 (51.7)	71 (48.3)	8.9 (5.6, 16.3)	66	34 (51.5)	32 (48.5)	5.4 (1.7, 9.8)	0.7143 (0.4752, 1.0737) 0.1056	0.1051	
North America	60	15 (25.0)	45 (75.0)	NE (8.3, NE)	33	11 (33.3)	22 (66.7)	4.5 (1.7, NE)	0.4857 (0.2181, 1.0817) 0.0771	0.0706	
Europe + Israel	166	61 (36.7)	105 (63.3)	NE (9.7, NE)	85	39 (45.9)	46 (54.1)	5.1 (2.8, NE)	0.5977 (0.3985, 0.8964) 0.0128	0.0121	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	200	84 (42.0)	116 (58.0)	14.1 (8.3, NE)	105	50 (47.6)	55 (52.4)	3.9 (1.7, 9.8)	0.5529 (0.3879, 0.7882) 0.0011	0.0009	0.2421
1	173	68 (39.3)	105 (60.7)	12.5 (8.8, NE)	79	34 (43.0)	45 (57.0)	6.1 (4.2, NE)	0.7481 (0.4937, 1.1337) 0.1712	0.1679	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.8599
0	60	24 (40.0)	36 (60.0)	12.5 (4.7, NE)	34	16 (47.1)	18 (52.9)	3.9 (1.4, NE)	0.5072 (0.2645, 0.9726) 0.0410	0.0376
1	108	44 (40.7)	64 (59.3)	12.5 (5.9, NE)	51	24 (47.1)	27 (52.9)	6.1 (1.5, NE)	0.6767 (0.4103, 1.1161) 0.1261	0.1255
2	115	43 (37.4)	72 (62.6)	NE (8.3, NE)	54	24 (44.4)	30 (55.6)	5.1 (2.1, NE)	0.5917 (0.3557, 0.9842) 0.0432	0.0414

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	41 (45.6)	49 (54.4)	12.8 (7.2, NE)	45	20 (44.4)	25 (55.6)	4.4 (2.8, NE)	0.7152 (0.4157, 1.2305) 0.2260	0.2238

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.9649
PD	174	64 (36.8)	110 (63.2)	16.3 (9.6, NE)	85	34 (40.0)	51 (60.0)	5.9 (2.9, NE)	0.6462 (0.4241, 0.9847) 0.0422	0.0408
PR	48	25 (52.1)	23 (47.9)	7.4 (4.2, NE)	22	9 (40.9)	13 (59.1)	4.3 (1.0, NE)	0.7177 (0.3331, 1.5461) 0.3969	0.3993
SD	82	36 (43.9)	46 (56.1)	12.5 (3.1, NE)	55	29 (52.7)	26 (47.3)	5.9 (1.7, 16.9)	0.6905 (0.4218, 1.1304) 0.1409	0.1400

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.0328
Yes	37	18 (48.6)	19 (51.4)	8.8 (2.8, NE)	15	3 (20.0)	12 (80.0)	NE (2.9, NE)	1.8357 (0.5371, 6.2745) 0.3327	0.3262	
No	336	134 (39.9)	202 (60.1)	13.9 (10.4, NE)	169	81 (47.9)	88 (52.1)	4.4 (2.8, 8.6)	0.5816 (0.4400, 0.7687) 0.0001	0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.2899
Yes	24	12 (50.0)	12 (50.0)	8.8 (3.0, NE)	8	3 (37.5)	5 (62.5)	5.9 (1.4, NE)	1.0117 (0.2834, 3.6122) 0.9857	0.9897	
No	349	140 (40.1)	209 (59.9)	13.9 (10.4, NE)	176	81 (46.0)	95 (54.0)	5.1 (2.8, 9.8)	0.6132 (0.4650, 0.8087) 0.0005	0.0005	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.1629
Normal Function	202	84 (41.6)	118 (58.4)	12.5 (7.4, NE)	87	47 (54.0)	40 (46.0)	2.8 (1.4, 5.9)	0.4739 (0.3297, 0.6812) 0.0001	<0.0001	
Mild Impairment	123	48 (39.0)	75 (61.0)	16.3 (9.7, NE)	69	28 (40.6)	41 (59.4)	4.3 (2.8, NE)	0.6339 (0.3928, 1.0230) 0.0619	0.0612	
Moderate Impairment	41	15 (36.6)	26 (63.4)	NE (4.2, NE)	23	8 (34.8)	15 (65.2)	16.9 (4.5, NE)	1.1196 (0.4734, 2.6482) 0.7970	0.7964	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.5112
Normal Function	170	73 (42.9)	97 (57.1)	13.8 (7.4, NE)	98	50 (51.0)	48 (49.0)	4.2 (1.7, 9.8)	0.5768 (0.4007, 0.8301) 0.0031	0.0027
Mild Impairment	195	76 (39.0)	119 (61.0)	14.1 (8.8, NE)	84	34 (40.5)	50 (59.5)	6.5 (2.7, NE)	0.6750 (0.4485, 1.0159) 0.0595	0.0609

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline visceral disease										0.0481
Yes	332	135 (40.7)	197 (59.3)	13.8 (9.6, NE)	157	66 (42.0)	91 (58.0)	6.1 (3.9, NE)	0.7074 (0.5258, 0.9516) 0.0221	0.0219
No	41	17 (41.5)	24 (58.5)	12.8 (3.0, NE)	27	18 (66.7)	9 (33.3)	1.7 (0.9, 4.5)	0.3395 (0.1672, 0.6894) 0.0028	0.0017

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.1413
Positive	331	138 (41.7)	193 (58.3)	13.8 (9.6, NE)	163	72 (44.2)	91 (55.8)	5.4 (3.9, 9.8)	0.6785 (0.5088, 0.9047) 0.0082	0.0080	
Negative	42	14 (33.3)	28 (66.7)	12.5 (5.0, NE)	21	12 (57.1)	9 (42.9)	1.5 (0.9, NE)	0.3490 (0.1573, 0.7742) 0.0096	0.0069	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (derived)										0.5989
Positive	333	138 (41.4)	195 (58.6)	13.8 (9.6, NE)	166	76 (45.8)	90 (54.2)	5.1 (3.0, 9.8)	0.6486 (0.4889, 0.8605)	0.0027
Negative	40	14 (35.0)	26 (65.0)	12.5 (5.0, NE)	18	8 (44.4)	10 (55.6)	5.9 (0.9, NE)	0.4738 (0.1939, 1.1574)	0.0928

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0526
HER2 IHC 1+	214	45 (21.0)	169 (79.0)	NE (NE, NE)	107	14 (13.1)	93 (86.9)	NE (NE, NE)	1.3706 (0.7508, 2.5023) 0.3046	0.3045	
HER2 IHC 2+/ISH Negative	159	33 (20.8)	126 (79.2)	NE (NE, NE)	77	20 (26.0)	57 (74.0)	NE (NE, NE)	0.6129 (0.3501, 1.0732) 0.0868	0.0842	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.1182
1	221	52 (23.5)	169 (76.5)	NE (NE, NE)	100	16 (16.0)	84 (84.0)	NE (NE, NE)	1.2182 (0.6946, 2.1365) 0.4912	0.4869
>=2	151	26 (17.2)	125 (82.8)	NE (NE, NE)	83	18 (21.7)	65 (78.3)	NE (NE, NE)	0.6458 (0.3521, 1.1845) 0.1577	0.1537

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.2828
Yes	235	51 (21.7)	184 (78.3)	NE (NE, NE)	118	24 (20.3)	94 (79.7)	NE (NE, NE)	0.7955 (0.4873, 1.2987) 0.3603	0.3571	
No	98	20 (20.4)	78 (79.6)	NE (NE, NE)	48	6 (12.5)	42 (87.5)	NE (NE, NE)	1.4732 (0.5914, 3.6701) 0.4054	0.4040	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3832
<65	290	66 (22.8)	224 (77.2)	NE (NE, NE)	136	29 (21.3)	107 (78.7)	NE (NE, NE)	0.8152 (0.5251, 1.2654) 0.3623	0.3612	
>=65	83	12 (14.5)	71 (85.5)	NE (NE, NE)	48	5 (10.4)	43 (89.6)	NE (NE, NE)	1.3707 (0.4825, 3.8942) 0.5539	0.5559	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Age										0.9276
<75	359	77 (21.4)	282 (78.6)	NE (NE, NE)	175	33 (18.9)	142 (81.1)	NE (NE, NE)	0.9042 (0.5999, 1.3629)	0.6291
>=75	14	1 (7.1)	13 (92.9)	NE (NE, NE)	9	1 (11.1)	8 (88.9)	NE (0.7, NE)	0.6305 (0.0442, 11.3185)	0.8055

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.0543
White	176	43 (24.4)	133 (75.6)	NE (NE, NE)	91	24 (26.4)	67 (73.6)	NE (4.5, NE)	0.6805 (0.4110, 1.1265) 0.1344	0.1316	
Non-White	197	35 (17.8)	162 (82.2)	NE (NE, NE)	92	9 (9.8)	83 (90.2)	NE (NE, NE)	1.6009 (0.7680, 3.3372) 0.2092	0.2024	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.3323
Asia	147	21 (14.3)	126 (85.7)	NE (NE, NE)	66	5 (7.6)	61 (92.4)	NE (NE, NE)	1.6515 (0.6213, 4.3896) 0.3145	0.3049	
North America	60	10 (16.7)	50 (83.3)	NE (NE, NE)	33	7 (21.2)	26 (78.8)	NE (2.7, NE)	0.6275 (0.2377, 1.6567) 0.3469	0.3383	
Europe + Israel	166	47 (28.3)	119 (71.7)	NE (NE, NE)	85	22 (25.9)	63 (74.1)	NE (7.0, NE)	0.8736 (0.5247, 1.4546) 0.6035	0.6023	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.4926
0	200	48 (24.0)	152 (76.0)	NE (NE, NE)	105	23 (21.9)	82 (78.1)	NE (NE, NE)	0.8259 (0.5010, 1.3614) 0.4531	0.4584	
1	173	30 (17.3)	143 (82.7)	NE (NE, NE)	79	11 (13.9)	68 (86.1)	NE (NE, NE)	1.1323 (0.5661, 2.2651) 0.7253	0.7288	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.0657
0	60	12 (20.0)	48 (80.0)	NE (NE, NE)	34	8 (23.5)	26 (76.5)	NE (3.4, NE)	0.6883 (0.2811, 1.6853)	0.4123
1	108	27 (25.0)	81 (75.0)	NE (NE, NE)	51	5 (9.8)	46 (90.2)	NE (NE, NE)	2.4837 (0.9556, 6.4554)	0.0534
2	115	23 (20.0)	92 (80.0)	NE (NE, NE)	54	12 (22.2)	42 (77.8)	NE (7.0, NE)	0.6724 (0.3315, 1.3640)	0.2605

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	16 (17.8)	74 (82.2)	NE (NE, NE)	45	9 (20.0)	36 (80.0)	NE (NE, NE)	0.6719 (0.2949, 1.5311) 0.3440	0.3402

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.1029
PD	174	44 (25.3)	130 (74.7)	NE (NE, NE)	85	19 (22.4)	66 (77.6)	NE (NE, NE)	0.9156 (0.5337, 1.5709) 0.7489	0.7493	
PR	48	5 (10.4)	43 (89.6)	NE (NE, NE)	22	5 (22.7)	17 (77.3)	NE (0.9, NE)	0.2249 (0.0627, 0.8074) 0.0221	0.0129	
SD	82	14 (17.1)	68 (82.9)	NE (NE, NE)	55	6 (10.9)	49 (89.1)	NE (NE, NE)	1.4752 (0.5655, 3.8483) 0.4268	0.4246	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.7592
Yes	37	9 (24.3)	28 (75.7)	NE (NE, NE)	15	3 (20.0)	12 (80.0)	NE (0.9, NE)	0.7649 (0.2056, 2.8453) 0.6893	0.6909	
No	336	69 (20.5)	267 (79.5)	NE (NE, NE)	169	31 (18.3)	138 (81.7)	NE (NE, NE)	0.9349 (0.6107, 1.4313) 0.7567	0.7561	

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 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.6686
Yes	24	5 (20.8)	19 (79.2)	NE (6.9, NE)	8	2 (25.0)	6 (75.0)	NE (0.9, NE)	0.5557 (0.1016, 3.0388) 0.4979	0.4917
No	349	73 (20.9)	276 (79.1)	NE (NE, NE)	176	32 (18.2)	144 (81.8)	NE (NE, NE)	0.9476 (0.6242, 1.4386) 0.8005	0.8011

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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[c] Two-sided p-value from unstratified log-rank test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.7109
Normal Function	202	46 (22.8)	156 (77.2)	NE (NE, NE)	87	19 (21.8)	68 (78.2)	NE (NE, NE)	0.7708 (0.4497, 1.3213) 0.3438	0.3418	
Mild Impairment	123	28 (22.8)	95 (77.2)	NE (NE, NE)	69	12 (17.4)	57 (82.6)	NE (NE, NE)	1.0875 (0.5513, 2.1452) 0.8089	0.8126	
Moderate Impairment	41	4 (9.8)	37 (90.2)	NE (NE, NE)	23	2 (8.7)	21 (91.3)	NE (NE, NE)	1.2821 (0.2344, 7.0136) 0.7744	0.7739	

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 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.5798
Normal Function	170	38 (22.4)	132 (77.6)	NE (NE, NE)	98	22 (22.4)	76 (77.6)	NE (NE, NE)	0.8634 (0.5096, 1.4629)	0.5779	
Mild Impairment	195	40 (20.5)	155 (79.5)	NE (NE, NE)	84	12 (14.3)	72 (85.7)	NE (NE, NE)	1.0378 (0.5418, 1.9878)	0.9073	

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline visceral disease										0.6982
Yes	332	65 (19.6)	267 (80.4)	NE (NE, NE)	157	27 (17.2)	130 (82.8)	NE (NE, NE)	0.9166 (0.5840, 1.4386) 0.7050	0.7052
No	41	13 (31.7)	28 (68.3)	NE (6.9, NE)	27	7 (25.9)	20 (74.1)	NE (4.5, NE)	1.0721 (0.4235, 2.7138) 0.8832	0.8860

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.5573
Positive	331	71 (21.5)	260 (78.5)	NE (NE, NE)	163	29 (17.8)	134 (82.2)	NE (NE, NE)	0.9589 (0.6212, 1.4802)	0.8499	0.8508
Negative	42	7 (16.7)	35 (83.3)	NE (NE, NE)	21	5 (23.8)	16 (76.2)	NE (3.4, NE)	0.7156 (0.2271, 2.2554)	0.5678	0.5667

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.6707
Positive	333	71 (21.3)	262 (78.7)	NE (NE, NE)	166	30 (18.1)	136 (81.9)	NE (NE, NE)	0.9451 (0.6154, 1.4515) 0.7964	0.7949	
Negative	40	7 (17.5)	33 (82.5)	NE (NE, NE)	18	4 (22.2)	14 (77.8)	NE (1.6, NE)	0.7637 (0.2235, 2.6098) 0.6673	0.6679	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.2742
HER2 IHC 1+	214	16 (7.5)	198 (92.5)	11.2 (1.7, NE)	107	5 (4.7)	102 (95.3)	NE (0.9, NE)	1.1752 (0.4206, 3.2835) 0.7581	0.7556	
HER2 IHC 2+/ISH Negative	159	17 (10.7)	142 (89.3)	7.1 (4.2, NE)	77	3 (3.9)	74 (96.1)	12.0 (NE, NE)	2.5097 (0.7331, 8.5918) 0.1428	0.1302	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.6423
1	221	19 (8.6)	202 (91.4)	11.2 (4.3, NE)	100	5 (5.0)	95 (95.0)	12.0 (NE, NE)	1.3228 (0.4875, 3.5893)	0.5733
>=2	151	14 (9.3)	137 (90.7)	5.6 (1.7, NE)	83	3 (3.6)	80 (96.4)	NE (2.3, NE)	2.4644 (0.7065, 8.5966)	0.1446

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Prior CDK4/6											
Yes	235	24 (10.2)	211 (89.8)	12.6 (4.3, NE)	118	4 (3.4)	114 (96.6)	NE (NE, NE)	2.1642 (0.7449, 6.2878)	0.1454	0.7542
No	98	7 (7.1)	91 (92.9)	11.2 (1.7, NE)	48	2 (4.2)	46 (95.8)	12.0 (0.8, NE)	1.4443 (0.2979, 7.0022)	0.6401	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7910
<65	290	28 (9.7)	262 (90.3)	11.2 (4.3, NE)	136	7 (5.1)	129 (94.9)	12.0 (NE, NE)	1.5720 (0.6795, 3.6369)	0.2887	
>=65	83	5 (6.0)	78 (94.0)	8.4 (1.0, NE)	48	1 (2.1)	47 (97.9)	NE (0.8, NE)	1.7501 (0.1940, 15.7860)	0.6134	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Age											
<75	359	32 (8.9)	327 (91.1)	11.2 (4.2, NE)	175	8 (4.6)	167 (95.4)	12.0 (NE, NE)	1.6509 (0.7543, 3.6132) 0.2097	0.2040	NE
>=75	14	1 (7.1)	13 (92.9)	8.4 (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.5461
White	176	17 (9.7)	159 (90.3)	12.6 (6.9, NE)	91	4 (4.4)	87 (95.6)	NE (NE, NE)	1.7208 (0.5713, 5.1836) 0.3346	0.3289	
Non-White	197	16 (8.1)	181 (91.9)	4.2 (0.8, NE)	92	4 (4.3)	88 (95.7)	12.0 (0.8, NE)	1.2389 (0.4132, 3.7150) 0.7022	0.6800	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.1960
Asia	147	8 (5.4)	139 (94.6)	2.9 (0.7, 11.2)	66	1 (1.5)	65 (98.5)	12.0 (NE, NE)	4.1825 (0.5151, 33.9632) 0.1805	0.1471	
North America	60	6 (10.0)	54 (90.0)	NE (2.1, NE)	33	0	33 (100)	NE (NE, NE)	NE (NE, NE) 0.9957	0.2447	
Europe + Israel	166	19 (11.4)	147 (88.6)	12.6 (4.2, NE)	85	7 (8.2)	78 (91.8)	NE (2.8, NE)	1.2381 (0.5143, 2.9803) 0.6337	0.6296	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.5145
0	200	18 (9.0)	182 (91.0)	12.6 (4.2, NE)	105	6 (5.7)	99 (94.3)	12.0 (NE, NE)	1.3030 (0.5067, 3.3506) 0.5828	0.5809	
1	173	15 (8.7)	158 (91.3)	6.9 (1.4, NE)	79	2 (2.5)	77 (97.5)	NE (2.8, NE)	2.6567 (0.6056, 11.6542) 0.1952	0.1792	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.7729
0	60	5 (8.3)	55 (91.7)	1.7 (0.7, NE)	34	3 (8.8)	31 (91.2)	12.0 (0.9, NE)	1.3971 (0.3306, 5.9043) 0.6493	0.6478	
1	108	12 (11.1)	96 (88.9)	5.6 (0.8, NE)	51	3 (5.9)	48 (94.1)	NE (0.8, NE)	1.4892 (0.4183, 5.3015) 0.5388	0.5109	
2	115	13 (11.3)	102 (88.7)	10.5 (3.0, NE)	54	1 (1.9)	53 (98.1)	NE (2.8, NE)	3.7651 (0.4836, 29.3157) 0.2055	0.1746	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	3 (3.3)	87 (96.7)	NE (11.2, NE)	45	1 (2.2)	44 (97.8)	NE (0.5, NE)	1.2902 (0.1167, 14.2652) 0.8354	0.8349

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.1044
PD	174	14 (8.0)	160 (92.0)	NE (4.1, NE)	85	6 (7.1)	79 (92.9)	NE (2.3, NE)	1.1126 (0.4251, 2.9123) 0.8279	0.8281	
PR	48	3 (6.3)	45 (93.8)	3.0 (0.8, NE)	22	0	22 (100)	NE (NE, NE)	NE (NE, NE) 0.9973	0.1362	
SD	82	9 (11.0)	73 (89.0)	4.9 (1.1, NE)	55	1 (1.8)	54 (98.2)	12.0 (NE, NE)	5.2224 (0.6567, 41.5302) 0.1182	0.0814	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.2226
Yes	37	4 (10.8)	33 (89.2)	6.9 (1.4, NE)	15	0	15 (100)	NE (NE, NE)	NE (NE, NE) 0.9977	0.3130	
No	336	29 (8.6)	307 (91.4)	11.2 (4.3, NE)	169	8 (4.7)	161 (95.3)	12.0 (NE, NE)	1.4763 (0.6681, 3.2618) 0.3355	0.3315	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										
Yes	24	1 (4.2)	23 (95.8)	NE (1.6, NE)	8	0	8 (100)	NE (NE, NE)	NE (NE, NE)	NE
No	349	32 (9.2)	317 (90.8)	8.4 (4.2, NE)	176	8 (4.5)	168 (95.5)	12.0 (NE, NE)	1.6708 (0.7629, 3.6590)	0.1937

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.5236
Normal Function	202	21 (10.4)	181 (89.6)	12.6 (3.0, NE)	87	6 (6.9)	81 (93.1)	12.0 (2.3, NE)	1.2365 (0.4927, 3.1029) 0.6511	0.6555	
Mild Impairment	123	9 (7.3)	114 (92.7)	8.3 (3.5, NE)	69	1 (1.4)	68 (98.6)	NE (NE, NE)	3.9376 (0.4975, 31.1636) 0.1941	0.1610	
Moderate Impairment	41	3 (7.3)	38 (92.7)	8.4 (1.6, NE)	23	1 (4.3)	22 (95.7)	NE (0.8, NE)	0.4714 (0.0283, 7.8580) 0.6004	0.5924	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.0490
Normal Function	170	12 (7.1)	158 (92.9)	NE (4.2, NE)	98	6 (6.1)	92 (93.9)	12.0 (1.8, NE)	0.8366 (0.3060, 2.2867)	0.7255	
Mild Impairment	195	21 (10.8)	174 (89.2)	6.9 (3.5, NE)	84	2 (2.4)	82 (97.6)	NE (NE, NE)	4.1522 (0.9700, 17.7737)	0.0366	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Baseline visceral disease											
Yes	332	27 (8.1)	305 (91.9)	8.3 (4.2, NE)	157	6 (3.8)	151 (96.2)	12.0 (NE, NE)	2.0668 (0.8479, 5.0380)	0.1009	0.1646
No	41	6 (14.6)	35 (85.4)	11.2 (0.7, NE)	27	2 (7.4)	25 (92.6)	2.3 (0.9, NE)	0.3327 (0.0429, 2.5779)	0.2712	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)										0.9150	
Positive	331	30 (9.1)	301 (90.9)	11.2 (4.4, NE)	163	6 (3.7)	157 (96.3)	12.0 (NE, NE)	1.8191 (0.7507, 4.4082)	0.1770	
Negative	42	3 (7.1)	39 (92.9)	1.3 (0.7, NE)	21	2 (9.5)	19 (90.5)	NE (0.9, NE)	2.1709 (0.3498, 13.4722)	0.3948	

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 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (derived)										0.8407
Positive	333	31 (9.3)	302 (90.7)	11.2 (4.3, NE)	166	6 (3.6)	160 (96.4)	12.0 (NE, NE)	1.9006 (0.7865, 4.5926) 0.1537	0.1451
Negative	40	2 (5.0)	38 (95.0)	1.1 (0.7, NE)	18	2 (11.1)	16 (88.9)	2.3 (0.9, NE)	1.4142 (0.1962, 10.1915) 0.7309	0.7297

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.2605
HER2 IHC 1+	214	75 (35.0)	139 (65.0)	17.3 (12.9, NE)	107	29 (27.1)	78 (72.9)	NE (11.1, NE)	0.9774 (0.6327, 1.5098) 0.9178	0.9184
HER2 IHC 2+/ISH Negative	159	56 (35.2)	103 (64.8)	NE (14.9, NE)	77	29 (37.7)	48 (62.3)	NE (4.4, NE)	0.7119 (0.4527, 1.1194) 0.1412	0.1399

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.0576
1	221	80 (36.2)	141 (63.8)	17.3 (12.7, NE)	100	28 (28.0)	72 (72.0)	NE (11.1, NE)	1.1160 (0.7230, 1.7225) 0.6204	0.6189
>=2	151	50 (33.1)	101 (66.9)	NE (13.3, NE)	83	30 (36.1)	53 (63.9)	NE (4.3, NE)	0.5747 (0.3621, 0.9123) 0.0188	0.0176

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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## Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.5219
Yes	235	77 (32.8)	158 (67.2)	23.6 (13.3, NE)	118	31 (26.3)	87 (73.7)	NE (NE, NE)	0.9461 (0.6201, 1.4436) 0.7972	0.7972	
No	98	40 (40.8)	58 (59.2)	16.6 (10.0, NE)	48	20 (41.7)	28 (58.3)	11.1 (5.7, NE)	0.7365 (0.4274, 1.2691) 0.2706	0.2693	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3727
<65	290	95 (32.8)	195 (67.2)	23.6 (16.9, NE)	136	41 (30.1)	95 (69.9)	NE (6.1, NE)	0.8165 (0.5640, 1.1818)	0.2830	
>=65	83	36 (43.4)	47 (56.6)	12.9 (8.2, NE)	48	17 (35.4)	31 (64.6)	11.3 (4.4, NE)	0.9888 (0.5509, 1.7747)	0.9702	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5355
<75	359	124 (34.5)	235 (65.5)	23.6 (16.3, NE)	175	54 (30.9)	121 (69.1)	NE (7.1, NE)	0.8495 (0.6150, 1.1735) 0.3225	0.3229	
>=75	14	7 (50.0)	7 (50.0)	13.3 (4.2, NE)	9	4 (44.4)	5 (55.6)	11.3 (0.7, NE)	1.0904 (0.3168, 3.7530) 0.8908	0.8908	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.8664
White	176	47 (26.7)	129 (73.3)	23.6 (23.6, NE)	91	21 (23.1)	70 (76.9)	NE (11.1, NE)	0.8638 (0.5115, 1.4586) 0.5838	0.5847	
Non-White	197	84 (42.6)	113 (57.4)	16.3 (8.3, NE)	92	37 (40.2)	55 (59.8)	7.7 (4.9, NE)	0.8119 (0.5496, 1.1994) 0.2952	0.2942	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Region										0.0874
Asia	147	63 (42.9)	84 (57.1)	16.9 (9.6, NE)	66	31 (47.0)	35 (53.0)	7.1 (3.5, NE)	0.6815 (0.4416, 1.0516)	0.0818
North America	60	12 (20.0)	48 (80.0)	NE (NE, NE)	33	9 (27.3)	24 (72.7)	NE (1.5, NE)	0.6093 (0.2551, 1.4554)	0.2615
Europe + Israel	166	56 (33.7)	110 (66.3)	23.6 (13.3, NE)	85	18 (21.2)	67 (78.8)	NE (11.1, NE)	1.2336 (0.7207, 2.1117)	0.4443

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	200	74 (37.0)	126 (63.0)	16.9 (13.3, NE)	105	37 (35.2)	68 (64.8)	11.1 (4.2, NE)	0.6695 (0.4485, 0.9992) 0.0496	0.0503	0.0890
1	173	57 (32.9)	116 (67.1)	NE (16.6, NE)	79	21 (26.6)	58 (73.4)	NE (11.3, NE)	1.1908 (0.7198, 1.9698) 0.4966	0.5027	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.9719
0	60	23 (38.3)	37 (61.7)	NE (3.1, NE)	34	13 (38.2)	21 (61.8)	7.1 (1.7, NE)	0.8053 (0.4071, 1.5928) 0.5337	0.5339	
1	108	30 (27.8)	78 (72.2)	17.3 (16.6, NE)	51	14 (27.5)	37 (72.5)	11.3 (7.7, NE)	0.8674 (0.4591, 1.6385) 0.6611	0.6622	
2	115	42 (36.5)	73 (63.5)	14.9 (11.2, NE)	54	16 (29.6)	38 (70.4)	NE (4.4, NE)	0.8716 (0.4833, 1.5717) 0.6477	0.6453	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	36 (40.0)	54 (60.0)	16.3 (8.3, NE)	45	15 (33.3)	30 (66.7)	NE (3.1, NE)	0.8634 (0.4683, 1.5916) 0.6378	0.6344

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.5708
PD	174	59 (33.9)	115 (66.1)	16.3 (14.1, NE)	85	20 (23.5)	65 (76.5)	NE (NE, NE)	1.0807 (0.6477, 1.8031) 0.7664	0.7630	
PR	48	20 (41.7)	28 (58.3)	NE (6.2, NE)	22	8 (36.4)	14 (63.6)	4.3 (2.9, NE)	0.7167 (0.3118, 1.6474) 0.4328	0.4336	
SD	82	31 (37.8)	51 (62.2)	NE (8.2, NE)	55	21 (38.2)	34 (61.8)	11.1 (4.9, NE)	0.7929 (0.4511, 1.3936) 0.4199	0.4201	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.3247
Yes	37	11 (29.7)	26 (70.3)	NE (7.1, NE)	15	5 (33.3)	10 (66.7)	4.3 (0.8, NE)	0.4529 (0.1525, 1.3449)	0.1425
No	336	120 (35.7)	216 (64.3)	17.3 (14.1, NE)	169	53 (31.4)	116 (68.6)	NE (11.1, NE)	0.8894 (0.6413, 1.2336)	0.4822

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.5562
Yes	24	8 (33.3)	16 (66.7)	NE (7.1, NE)	8	3 (37.5)	5 (62.5)	NE (0.8, NE)	0.4854 (0.1248, 1.8875) 0.2969	0.2870
No	349	123 (35.2)	226 (64.8)	17.3 (14.9, NE)	176	55 (31.3)	121 (68.8)	NE (7.7, NE)	0.8741 (0.6337, 1.2058) 0.4123	0.4119

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Renal function at baseline										0.6115
Normal Function	202	66 (32.7)	136 (67.3)	23.6 (23.6, NE)	87	22 (25.3)	65 (74.7)	NE (NE, NE)	0.9912 (0.6089, 1.6136) 0.9716	0.9766
Mild Impairment	123	46 (37.4)	77 (62.6)	16.3 (10.0, NE)	69	26 (37.7)	43 (62.3)	7.1 (2.9, NE)	0.7191 (0.4408, 1.1731) 0.1866	0.1842
Moderate Impairment	41	17 (41.5)	24 (58.5)	13.3 (7.1, NE)	23	9 (39.1)	14 (60.9)	11.3 (5.9, NE)	1.0318 (0.4584, 2.3224) 0.9397	0.9456

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.4428
Normal Function	170	69 (40.6)	101 (59.4)	16.3 (10.8, NE)	98	32 (32.7)	66 (67.3)	NE (6.1, NE)	0.9584 (0.6269, 1.4652) 0.8444	0.8409
Mild Impairment	195	60 (30.8)	135 (69.2)	NE (16.6, NE)	84	25 (29.8)	59 (70.2)	NE (11.3, NE)	0.7638 (0.4765, 1.2243) 0.2630	0.2630

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.8983
Yes	332	115 (34.6)	217 (65.4)	17.3 (14.1, NE)	157	50 (31.8)	107 (68.2)	NE (11.1, NE)	0.8422 (0.6024, 1.1772) 0.3148	0.3154	
No	41	16 (39.0)	25 (61.0)	23.6 (3.0, NE)	27	8 (29.6)	19 (70.4)	5.9 (4.9, NE)	0.9942 (0.4199, 2.3541) 0.9894	0.9887	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (IXRS)										0.6247
Positive	331	116 (35.0)	215 (65.0)	17.3 (14.9, NE)	163	50 (30.7)	113 (69.3)	NE (11.1, NE)	0.8614 (0.6159, 1.2046) 0.3831	0.3829
Negative	42	15 (35.7)	27 (64.3)	NE (2.8, NE)	21	8 (38.1)	13 (61.9)	5.9 (1.4, NE)	0.8125 (0.3438, 1.9199) 0.6359	0.6305

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (derived)										0.4497
Positive	333	117 (35.1)	216 (64.9)	17.3 (14.9, NE)	166	51 (30.7)	115 (69.3)	NE (11.1, NE)	0.8691 (0.6231, 1.2122) 0.4086	0.4080
Negative	40	14 (35.0)	26 (65.0)	NE (2.9, NE)	18	7 (38.9)	11 (61.1)	5.9 (1.4, NE)	0.7088 (0.2853, 1.7609) 0.4585	0.4540

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.3561
HER2 IHC 1+	214	117 (54.7)	97 (45.3)	4.2 (2.8, 7.1)	107	60 (56.1)	47 (43.9)	2.1 (1.4, 4.7)	0.7385 (0.5402, 1.0097) 0.0575	0.0584	
HER2 IHC 2+/ISH Negative	159	94 (59.1)	65 (40.9)	4.2 (2.8, 6.2)	77	41 (53.2)	36 (46.8)	3.9 (1.7, 6.7)	0.9310 (0.6438, 1.3463) 0.7041	0.6907	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.7319
1	221	131 (59.3)	90 (40.7)	2.9 (2.8, 5.3)	100	59 (59.0)	41 (41.0)	2.8 (1.4, 4.7)	0.8396 (0.6168, 1.1428) 0.2664	0.2630
>=2	151	79 (52.3)	72 (47.7)	6.3 (3.6, 11.2)	83	42 (50.6)	41 (49.4)	3.9 (1.5, 8.5)	0.7514 (0.5144, 1.0976) 0.1394	0.1352

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.8368
Yes	235	133 (56.6)	102 (43.4)	4.1 (2.8, 6.2)	118	65 (55.1)	53 (44.9)	3.6 (1.4, 6.7)	0.7958 (0.5906, 1.0722) 0.1332	0.1308	
No	98	58 (59.2)	40 (40.8)	5.1 (2.8, 9.7)	48	29 (60.4)	19 (39.6)	2.9 (1.4, 7.5)	0.7658 (0.4898, 1.1972) 0.2418	0.2457	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6300
<65	290	162 (55.9)	128 (44.1)	4.2 (2.8, 7.1)	136	72 (52.9)	64 (47.1)	2.9 (1.4, 5.9)	0.7895 (0.5969, 1.0443) 0.0977	0.0954	
>=65	83	49 (59.0)	34 (41.0)	4.2 (1.9, 6.7)	48	29 (60.4)	19 (39.6)	4.2 (1.5, 7.0)	0.9106 (0.5738, 1.4451) 0.6911	0.7006	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0637
<75	359	201 (56.0)	158 (44.0)	4.2 (2.9, 6.7)	175	96 (54.9)	79 (45.1)	2.8 (1.5, 4.5)	0.7693 (0.6022, 0.9828) 0.0358	0.0349	
>=75	14	10 (71.4)	4 (28.6)	2.8 (1.4, 4.2)	9	5 (55.6)	4 (44.4)	15.8 (1.4, NE)	2.3968 (0.7879, 7.2909) 0.1236	0.1101	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.7272
White	176	98 (55.7)	78 (44.3)	2.8 (2.2, 6.2)	91	47 (51.6)	44 (48.4)	2.8 (1.4, 11.4)	0.8559 (0.6041, 1.2128) 0.3817	0.3757	
Non-White	197	113 (57.4)	84 (42.6)	5.0 (2.9, 8.3)	92	54 (58.7)	38 (41.3)	3.6 (1.5, 5.9)	0.7658 (0.5521, 1.0621) 0.1099	0.1087	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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## Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.4028
Asia	147	91 (61.9)	56 (38.1)	4.3 (2.9, 6.7)	66	42 (63.6)	24 (36.4)	2.7 (1.5, 5.9)	0.7721 (0.5344, 1.1157) 0.1685	0.1666	
North America	60	27 (45.0)	33 (55.0)	5.7 (2.2, NE)	33	17 (51.5)	16 (48.5)	1.6 (1.1, 4.5)	0.5687 (0.3070, 1.0534) 0.0727	0.0680	
Europe + Israel	166	93 (56.0)	73 (44.0)	2.8 (1.9, 7.1)	85	42 (49.4)	43 (50.6)	4.2 (1.5, 15.5)	0.9619 (0.6675, 1.3862) 0.8349	0.8307	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	200	120 (60.0)	80 (40.0)	3.6 (2.8, 6.3)	105	60 (57.1)	45 (42.9)	1.9 (1.4, 4.4)	0.7457 (0.5459, 1.0188) 0.0653	0.0653	0.4721
1	173	91 (52.6)	82 (47.4)	4.2 (2.8, 7.3)	79	41 (51.9)	38 (48.1)	4.2 (1.7, 8.5)	0.9074 (0.6266, 1.3139) 0.6068	0.5968	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.6085
0	60	37 (61.7)	23 (38.3)	2.8 (1.5, 6.7)	34	18 (52.9)	16 (47.1)	1.7 (1.4, 5.9)	0.8983 (0.5082, 1.5881) 0.7123	0.7032	
1	108	57 (52.8)	51 (47.2)	5.0 (2.8, 7.7)	51	25 (49.0)	26 (51.0)	6.1 (2.7, 15.8)	0.9946 (0.6212, 1.5926) 0.9821	0.9805	
2	115	67 (58.3)	48 (41.7)	4.2 (2.3, 8.3)	54	34 (63.0)	20 (37.0)	1.6 (1.1, 4.5)	0.6641 (0.4377, 1.0079) 0.0545	0.0523	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	50 (55.6)	40 (44.4)	4.3 (2.0, 23.0)	45	24 (53.3)	21 (46.7)	4.2 (1.2, NE)	0.7931 (0.4844, 1.2985) 0.3567	0.3514

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy									0.7047
PD	174	90 (51.7)	84 (48.3) (2.8, 8.5)	85	44 (51.8)	41 (48.2) (1.4, 7.5)	0.7160 (0.4984, 1.0286) 0.0707	0.0683	
PR	48	29 (60.4)	19 (39.6) (1.4, 11.2)	22	11 (50.0)	11 (50.0) (0.9, NE)	0.9787 (0.4876, 1.9641) 0.9516	0.9502	
SD	82	48 (58.5)	34 (41.5) (2.8, 7.1)	55	33 (60.0)	22 (40.0) (1.5, 11.4)	0.8484 (0.5437, 1.3239) 0.4691	0.4745	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.5870
Yes	37	18 (48.6)	19 (51.4)	7.1 (2.8, NE)	15	6 (40.0)	9 (60.0)	1.7 (0.8, NE)	0.6101 (0.2394, 1.5545) 0.3004	0.2931
No	336	193 (57.4)	143 (42.6)	4.1 (2.8, 5.6)	169	95 (56.2)	74 (43.8)	3.1 (1.6, 4.7)	0.8368 (0.6537, 1.0713) 0.1575	0.1561

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.7868
Yes	24	9 (37.5)	15 (62.5)	NE (2.9, NE)	8	3 (37.5)	5 (62.5)	NE (0.8, NE)	0.6838 (0.1833, 2.5505) 0.5714	0.5730
No	349	202 (57.9)	147 (42.1)	4.1 (2.8, 5.6)	176	98 (55.7)	78 (44.3)	3.1 (1.6, 4.5)	0.8288 (0.6503, 1.0563) 0.1292	0.1276

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.8127
Normal Function	202	114 (56.4)	88 (43.6)	3.6 (2.8, 7.3)	87	47 (54.0)	40 (46.0)	3.1 (1.4, 4.4)	0.7774 (0.5516, 1.0957) 0.1504	0.1440	
Mild Impairment	123	72 (58.5)	51 (41.5)	4.1 (2.8, 6.7)	69	38 (55.1)	31 (44.9)	2.8 (1.4, 6.7)	0.8282 (0.5571, 1.2312) 0.3515	0.3518	
Moderate Impairment	41	22 (53.7)	19 (46.3)	4.2 (2.3, NE)	23	13 (56.5)	10 (43.5)	5.9 (1.5, NE)	0.9931 (0.4998, 1.9733) 0.9843	0.9861	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.3729
Normal Function	170	111 (65.3)	59 (34.7)	2.8 (1.7, 4.2)	98	58 (59.2)	40 (40.8)	2.7 (1.5, 4.5)	0.9369 (0.6811, 1.2889) 0.6890	0.6737
Mild Impairment	195	97 (49.7)	98 (50.3)	6.7 (3.4, 10.6)	84	41 (48.8)	43 (51.2)	4.2 (1.5, 8.5)	0.7454 (0.5161, 1.0766) 0.1172	0.1148

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.6210
Yes	332	189 (56.9)	143 (43.1)	4.2 (2.9, 5.9)	157	85 (54.1)	72 (45.9)	2.9 (1.5, 6.1)	0.8270 (0.6397, 1.0693) 0.1474	0.1471	
No	41	22 (53.7)	19 (46.3)	2.8 (1.7, NE)	27	16 (59.3)	11 (40.7)	3.9 (1.5, 6.7)	0.6887 (0.3581, 1.3244) 0.2637	0.2552	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.6494
Positive	331	189 (57.1)	142 (42.9)	4.2 (2.9, 5.9)	163	90 (55.2)	73 (44.8)	2.9 (1.5, 4.7)	0.7970 (0.6194, 1.0255) 0.0776	0.0781	
Negative	42	22 (52.4)	20 (47.6)	2.8 (1.6, NE)	21	11 (52.4)	10 (47.6)	4.4 (1.5, NE)	0.9778 (0.4703, 2.0331) 0.9522	0.9370	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.2600
Positive	333	190 (57.1)	143 (42.9)	4.2 (2.8, 5.9)	166	94 (56.6)	72 (43.4)	2.9 (1.5, 4.4)	0.7785 (0.6074, 0.9979) 0.0481	0.0479	
Negative	40	21 (52.5)	19 (47.5)	2.9 (1.5, NE)	18	7 (38.9)	11 (61.1)	5.9 (1.5, NE)	1.3242 (0.5586, 3.1388) 0.5237	0.5224	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.8752
HER2 IHC 1+	214	60 (28.0)	154 (72.0)	NE (20.3, NE)	107	23 (21.5)	84 (78.5)	NE (NE, NE)	1.0018 (0.6165, 1.6279) 0.9942	0.9943	
HER2 IHC 2+/ISH Negative	159	39 (24.5)	120 (75.5)	NE (17.1, NE)	77	15 (19.5)	62 (80.5)	NE (NE, NE)	0.8276 (0.4522, 1.5148) 0.5396	0.5385	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.0771
1	221	63 (28.5)	158 (71.5)	NE (20.3, NE)	100	18 (18.0)	82 (82.0)	NE (NE, NE)	1.2855 (0.7593, 2.1763) 0.3498	0.3478
>=2	151	36 (23.8)	115 (76.2)	NE (17.1, NE)	83	20 (24.1)	63 (75.9)	NE (8.1, NE)	0.5897 (0.3353, 1.0370) 0.0667	0.0640

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.2777
Yes	235	64 (27.2)	171 (72.8)	NE (NE, NE)	118	23 (19.5)	95 (80.5)	NE (NE, NE)	1.0510 (0.6498, 1.6999) 0.8394	0.8410	
No	98	24 (24.5)	74 (75.5)	NE (20.3, NE)	48	12 (25.0)	36 (75.0)	NE (8.1, NE)	0.6303 (0.3100, 1.2813) 0.2022	0.1991	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0045
<65	290	74 (25.5)	216 (74.5)	NE (NE, NE)	136	33 (24.3)	103 (75.7)	NE (8.5, NE)	0.6653 (0.4386, 1.0090) 0.0551	0.0536	
>=65	83	25 (30.1)	58 (69.9)	20.3 (17.1, NE)	48	5 (10.4)	43 (89.6)	NE (NE, NE)	2.7523 (1.0444, 7.2533) 0.0406	0.0327	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6720
<75	359	97 (27.0)	262 (73.0)	NE (20.3, NE)	175	37 (21.1)	138 (78.9)	NE (NE, NE)	0.8809 (0.5999, 1.2936) 0.5177	0.5167	
>=75	14	2 (14.3)	12 (85.7)	NE (1.6, NE)	9	1 (11.1)	8 (88.9)	NE (1.4, NE)	1.5289 (0.1385, 16.8724) 0.7289	0.7269	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.4872
White	176	41 (23.3)	135 (76.7)	NE (NE, NE)	91	18 (19.8)	73 (80.2)	NE (NE, NE)	0.7906 (0.4507, 1.3869) 0.4126	0.4107	
Non-White	197	58 (29.4)	139 (70.6)	NE (17.1, NE)	92	20 (21.7)	72 (78.3)	NE (NE, NE)	1.0348 (0.6191, 1.7297) 0.8962	0.8969	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.7736
Asia	147	43 (29.3)	104 (70.7)	NE (17.1, NE)	66	16 (24.2)	50 (75.8)	NE (8.5, NE)	0.8732 (0.4884, 1.5612) 0.6475	0.6453	
North America	60	14 (23.3)	46 (76.7)	NE (7.8, NE)	33	4 (12.1)	29 (87.9)	NE (NE, NE)	1.3579 (0.4414, 4.1780) 0.5936	0.5907	
Europe + Israel	166	42 (25.3)	124 (74.7)	NE (NE, NE)	85	18 (21.2)	67 (78.8)	NE (NE, NE)	0.8656 (0.4947, 1.5146) 0.6132	0.6111	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.6429
0	200	54 (27.0)	146 (73.0)	NE (20.3, NE)	105	22 (21.0)	83 (79.0)	NE (NE, NE)	0.8504 (0.5150, 1.4042) 0.5264	0.5271	
1	173	45 (26.0)	128 (74.0)	NE (14.7, NE)	79	16 (20.3)	63 (79.7)	NE (8.5, NE)	1.0286 (0.5769, 1.8339) 0.9239	0.9264	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.2874
0	60	18 (30.0)	42 (70.0)	NE (7.4, NE)	34	7 (20.6)	27 (79.4)	NE (5.8, NE)	1.0000 (0.4153, 2.4080)	0.9961
1	108	26 (24.1)	82 (75.9)	NE (NE, NE)	51	8 (15.7)	43 (84.3)	NE (NE, NE)	1.4197 (0.6413, 3.1428)	0.3854
2	115	30 (26.1)	85 (73.9)	NE (NE, NE)	54	15 (27.8)	39 (72.2)	NE (4.2, NE)	0.5662 (0.2978, 1.0764)	0.0785

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	25 (27.8)	65 (72.2)	17.1 (14.7, NE)	45	8 (17.8)	37 (82.2)	NE (NE, NE)	0.9826 (0.4353, 2.2177) 0.9662	0.9658	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.3467
PD	174	43 (24.7)	131 (75.3)	NE (16.3, NE)	85	17 (20.0)	68 (80.0)	NE (NE, NE)	0.7963 (0.4479, 1.4159) 0.4379	0.4369	
PR	48	13 (27.1)	35 (72.9)	NE (14.7, NE)	22	6 (27.3)	16 (72.7)	NE (3.0, NE)	0.6764 (0.2517, 1.8177) 0.4383	0.4327	
SD	82	21 (25.6)	61 (74.4)	NE (20.3, NE)	55	8 (14.5)	47 (85.5)	NE (NE, NE)	1.4707 (0.6475, 3.3403) 0.3567	0.3543	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.2081
Yes	37	11 (29.7)	26 (70.3)	NE (8.3, NE)	15	1 (6.7)	14 (93.3)	NE (3.0, NE)	2.1113 (0.2636, 16.9086) 0.4814	0.4716
No	336	88 (26.2)	248 (73.8)	NE (20.3, NE)	169	37 (21.9)	132 (78.1)	NE (NE, NE)	0.8720 (0.5909, 1.2868) 0.4902	0.4894

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.7947
Yes	24	5 (20.8)	19 (79.2)	NE (9.3, NE)	8	1 (12.5)	7 (87.5)	NE (3.0, NE)	0.7218 (0.0780, 6.6828) 0.7740	0.7734	
No	349	94 (26.9)	255 (73.1)	NE (20.3, NE)	176	37 (21.0)	139 (79.0)	NE (NE, NE)	0.9289 (0.6320, 1.3654) 0.7075	0.7067	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Renal function at baseline										0.0053
Normal Function	202	52 (25.7)	150 (74.3)	NE (20.3, NE)	87	19 (21.8)	68 (78.2)	NE (NE, NE)	0.7424 (0.4358, 1.2646) 0.2731	0.2719
Mild Impairment	123	33 (26.8)	90 (73.2)	NE (16.3, NE)	69	17 (24.6)	52 (75.4)	NE (7.1, NE)	0.7017 (0.3843, 1.2810) 0.2486	0.2462
Moderate Impairment	41	13 (31.7)	28 (68.3)	NE (11.8, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	8.5583 (1.1161, 65.6263) 0.0389	0.0131

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.3598
Normal Function	170	54 (31.8)	116 (68.2)	NE (16.3, NE)	98	21 (21.4)	77 (78.6)	NE (NE, NE)	1.1337 (0.6814, 1.8864) 0.6290	0.6301	
Mild Impairment	195	44 (22.6)	151 (77.4)	NE (NE, NE)	84	16 (19.0)	68 (81.0)	NE (NE, NE)	0.7599 (0.4243, 1.3608) 0.3556	0.3547	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.2437
Yes	332	85 (25.6)	247 (74.4)	NE (20.3, NE)	157	29 (18.5)	128 (81.5)	NE (NE, NE)	1.0225 (0.6679, 1.5652) 0.9186	0.9189	
No	41	14 (34.1)	27 (65.9)	NE (6.5, NE)	27	9 (33.3)	18 (66.7)	NE (3.1, NE)	0.6017 (0.2515, 1.4398) 0.2538	0.2477	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.8177
Positive	331	88 (26.6)	243 (73.4)	NE (20.3, NE)	163	34 (20.9)	129 (79.1)	NE (NE, NE)	0.9258 (0.6205, 1.3812) 0.7055	0.7045	
Negative	42	11 (26.2)	31 (73.8)	17.1 (9.3, NE)	21	4 (19.0)	17 (81.0)	NE (5.8, NE)	0.8286 (0.2495, 2.7511) 0.7587	0.7584	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.5139
Positive	333	87 (26.1)	246 (73.9)	NE (20.3, NE)	166	35 (21.1)	131 (78.9)	NE (NE, NE)	0.8990 (0.6045, 1.3370) 0.5990	0.5977	
Negative	40	12 (30.0)	28 (70.0)	17.1 (9.3, NE)	18	3 (16.7)	15 (83.3)	NE (5.8, NE)	1.1066 (0.2997, 4.0866) 0.8792	0.8792	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.9805
HER2 IHC 1+	214	101 (47.2)	113 (52.8)	8.3 (6.7, 11.2)	107	45 (42.1)	62 (57.9)	5.4 (2.1, NE)	0.7350 (0.5147, 1.0497) 0.0904	0.0899	
HER2 IHC 2+/ISH Negative	159	78 (49.1)	81 (50.9)	8.3 (5.6, 14.1)	77	36 (46.8)	41 (53.2)	4.7 (2.8, NE)	0.7549 (0.5056, 1.1272) 0.1693	0.1672	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.1075
1	221	116 (52.5)	105 (47.5)	6.7 (4.3, 8.4)	100	45 (45.0)	55 (55.0)	5.1 (2.2, NE)	0.9161 (0.6478, 1.2956)	0.6116
>=2	151	63 (41.7)	88 (58.3)	11.8 (7.6, NE)	83	36 (43.4)	47 (56.6)	5.4 (2.1, NE)	0.5149 (0.3369, 0.7870)	0.0019

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.1243
Yes	235	113 (48.1)	122 (51.9)	7.7 (5.8, 11.2)	118	44 (37.3)	74 (62.7)	5.4 (3.3, NE)	0.9290 (0.6526, 1.3223) 0.6825	0.6770	
No	98	50 (51.0)	48 (49.0)	7.5 (5.6, 14.1)	48	28 (58.3)	20 (41.7)	3.3 (1.4, 7.0)	0.5497 (0.3440, 0.8783) 0.0123	0.0112	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5051
<65	290	143 (49.3)	147 (50.7)	7.7 (6.9, 11.2)	136	57 (41.9)	79 (58.1)	5.1 (3.1, NE)	0.7874 (0.5762, 1.0759) 0.1334	0.1317	
>=65	83	36 (43.4)	47 (56.6)	8.3 (4.9, NE)	48	24 (50.0)	24 (50.0)	4.5 (1.5, NE)	0.6321 (0.3750, 1.0653) 0.0850	0.0833	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5854
<75	359	174 (48.5)	185 (51.5)	7.7 (6.9, 11.2)	175	76 (43.4)	99 (56.6)	5.1 (3.1, 7.1)	0.7508 (0.5708, 0.9875) 0.0403	0.0393	
>=75	14	5 (35.7)	9 (64.3)	NE (2.8, NE)	9	5 (55.6)	4 (44.4)	3.3 (0.7, NE)	0.5064 (0.1453, 1.7646) 0.2854	0.2848	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.8187
White	176	80 (45.5)	96 (54.5)	8.3 (6.7, 11.2)	91	36 (39.6)	55 (60.4)	5.1 (3.8, NE)	0.7334 (0.4916, 1.0944) 0.1289	0.1270	
Non-White	197	99 (50.3)	98 (49.7)	9.7 (5.3, 13.8)	92	45 (48.9)	47 (51.1)	3.3 (2.1, NE)	0.7342 (0.5132, 1.0505) 0.0909	0.0894	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.7376
Asia	147	85 (57.8)	62 (42.2)	7.1 (4.3, 11.2)	66	35 (53.0)	31 (47.0)	2.8 (1.6, NE)	0.7574 (0.5081, 1.1291) 0.1726	0.1718	
North America	60	22 (36.7)	38 (63.3)	8.4 (4.5, NE)	33	13 (39.4)	20 (60.6)	3.7 (1.6, NE)	0.4522 (0.2196, 0.9312) 0.0313	0.0278	
Europe + Israel	166	72 (43.4)	94 (56.6)	9.3 (7.0, NE)	85	33 (38.8)	52 (61.2)	6.3 (3.8, NE)	0.7959 (0.5245, 1.2077) 0.2833	0.2812	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	200	105 (52.5)	95 (47.5)	7.7 (5.6, 11.2)	105	50 (47.6)	55 (52.4)	3.1 (1.7, 5.1)	0.6202 (0.4391, 0.8762) 0.0067	0.0062	0.1522
1	173	74 (42.8)	99 (57.2)	8.5 (5.9, NE)	79	31 (39.2)	48 (60.8)	7.1 (4.5, NE)	0.9356 (0.6136, 1.4265) 0.7570	0.7628	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.2126
0	60	29 (48.3)	31 (51.7)	9.7 (4.9, 14.1)	34	18 (52.9)	16 (47.1)	1.7 (1.4, 5.9)	0.4244 (0.2260, 0.7967) 0.0077	0.0064
1	108	45 (41.7)	63 (58.3)	8.5 (5.9, NE)	51	22 (43.1)	29 (56.9)	6.1 (1.9, NE)	0.7641 (0.4587, 1.2730) 0.3015	0.3004
2	115	54 (47.0)	61 (53.0)	8.3 (5.1, NE)	54	25 (46.3)	29 (53.7)	4.5 (1.5, NE)	0.6695 (0.4106, 1.0918) 0.1078	0.1055

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	51 (56.7)	39 (43.3)	7.0 (2.9, 11.8)	45	16 (35.6)	29 (64.4)	NE (2.8, NE)	1.1731 (0.6635, 2.0739) 0.5830	0.5765

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.9224
PD	174	66 (37.9)	108 (62.1)	13.4 (7.1, NE)	85	30 (35.3)	55 (64.7)	5.9 (3.7, NE)	0.7606 (0.4910, 1.1782) 0.2203	0.2172	
PR	48	28 (58.3)	20 (41.7)	9.3 (4.3, 11.2)	22	11 (50.0)	11 (50.0)	4.0 (1.0, NE)	0.6112 (0.2988, 1.2502) 0.1775	0.1691	
SD	82	43 (52.4)	39 (47.6)	7.3 (4.4, 16.9)	55	29 (52.7)	26 (47.3)	3.1 (1.4, NE)	0.6676 (0.4139, 1.0768) 0.0976	0.0976	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.0664
Yes	37	17 (45.9)	20 (54.1)	11.2 (4.9, NE)	15	2 (13.3)	13 (86.7)	NE (1.6, NE)	2.0536 (0.4662, 9.0456) 0.3415	0.3297
No	336	162 (48.2)	174 (51.8)	8.3 (6.9, 11.2)	169	79 (46.7)	90 (53.3)	4.7 (2.8, 6.3)	0.7088 (0.5394, 0.9315) 0.0135	0.0131

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.2166
Yes	24	12 (50.0)	12 (50.0)	7.1 (4.9, NE)	8	2 (25.0)	6 (75.0)	NE (1.6, NE)	1.4977 (0.3313, 6.7702) 0.5997	0.5913	
No	349	167 (47.9)	182 (52.1)	8.3 (7.0, 11.2)	176	79 (44.9)	97 (55.1)	4.7 (2.8, 7.0)	0.7234 (0.5511, 0.9495) 0.0196	0.0191	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.9025
Normal Function	202	96 (47.5)	106 (52.5)	7.5 (6.2, 14.1)	87	36 (41.4)	51 (58.6)	5.1 (2.9, NE)	0.7759 (0.5255, 1.1456) 0.2019	0.1963	
Mild Impairment	123	62 (50.4)	61 (49.6)	8.3 (4.4, 11.8)	69	31 (44.9)	38 (55.1)	6.1 (1.6, 7.1)	0.6396 (0.4078, 1.0033) 0.0517	0.0504	
Moderate Impairment	41	18 (43.9)	23 (56.1)	11.2 (4.4, NE)	23	12 (52.2)	11 (47.8)	4.7 (1.5, NE)	0.7583 (0.3646, 1.5771) 0.4589	0.4617	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.4294
Normal Function	170	93 (54.7)	77 (45.3)	7.0 (4.9, 11.2)	98	51 (52.0)	47 (48.0)	3.7 (1.7, 6.1)	0.7108 (0.5023, 1.0058) 0.0539	0.0517	
Mild Impairment	195	84 (43.1)	111 (56.9)	8.5 (7.1, NE)	84	28 (33.3)	56 (66.7)	NE (3.8, NE)	0.8876 (0.5757, 1.3686) 0.5895	0.5967	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.0425
Yes	332	159 (47.9)	173 (52.1)	8.3 (7.0, 11.2)	157	64 (40.8)	93 (59.2)	6.1 (3.3, NE)	0.8240 (0.6144, 1.1051) 0.1962	0.1964	
No	41	20 (48.8)	21 (51.2)	6.7 (1.5, NE)	27	17 (63.0)	10 (37.0)	1.6 (1.0, 4.5)	0.4700 (0.2392, 0.9236) 0.0285	0.0237	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.1536
Positive	331	163 (49.2)	168 (50.8)	7.7 (6.9, 11.2)	163	70 (42.9)	93 (57.1)	5.4 (3.1, NE)	0.7939 (0.5979, 1.0542)	0.1107	0.1094
Negative	42	16 (38.1)	26 (61.9)	11.2 (2.8, NE)	21	11 (52.4)	10 (47.6)	3.1 (1.0, NE)	0.4434 (0.1969, 0.9985)	0.0433	0.0496

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.3151
Positive	333	162 (48.6)	171 (51.4)	8.3 (6.9, 11.2)	166	72 (43.4)	94 (56.6)	5.1 (3.1, NE)	0.7754 (0.5853, 1.0273) 0.0763	0.0748	
Negative	40	17 (42.5)	23 (57.5)	10.0 (2.8, NE)	18	9 (50.0)	9 (50.0)	1.7 (0.9, NE)	0.4925 (0.2114, 1.1473) 0.1007	0.0937	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.8248
HER2 IHC 1+	214	23 (10.7)	191 (89.3)	7.2 (1.6, NE)	107	8 (7.5)	99 (92.5)	NE (0.8, NE)	0.9382 (0.4174, 2.1087)	0.8786
HER2 IHC 2+/ISH Negative	159	19 (11.9)	140 (88.1)	9.7 (2.9, NE)	77	8 (10.4)	69 (89.6)	NE (1.0, NE)	0.7753 (0.3338, 1.8006)	0.5569

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.9367
1	221	30 (13.6)	191 (86.4)	5.6 (1.6, 9.9)	100	12 (12.0)	88 (88.0)	2.1 (1.0, NE)	0.8794 (0.4455, 1.7359)	0.7139
>=2	151	12 (7.9)	139 (92.1)	NE (7.4, NE)	83	4 (4.8)	79 (95.2)	NE (0.7, NE)	0.8699 (0.2788, 2.7144)	0.8058

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Prior CDK4/6											0.3854
Yes	235	25 (10.6)	210 (89.4)	9.9 (2.9, NE)	118	8 (6.8)	110 (93.2)	NE (1.2, NE)	0.9499 (0.4219, 2.1385) 0.9012	0.9042	
No	98	13 (13.3)	85 (86.7)	4.3 (1.3, NE)	48	7 (14.6)	41 (85.4)	1.5 (0.7, NE)	0.6398 (0.2532, 1.6166) 0.3450	0.3322	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Age										0.8282
<65	290	34 (11.7)	256 (88.3)	7.4 (2.9, NE)	136	10 (7.4)	126 (92.6)	NE (1.0, NE)	0.8764 (0.4301, 1.7860)	0.7105
>=65	83	8 (9.6)	75 (90.4)	6.7 (0.9, NE)	48	6 (12.5)	42 (87.5)	2.8 (0.7, NE)	0.8927 (0.3069, 2.5965)	0.8407

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0530
<75	359	40 (11.1)	319 (88.9)	9.7 (3.0, NE)	175	16 (9.1)	159 (90.9)	NE (1.2, NE)	0.7847 (0.4359, 1.4125) 0.4188	0.4189	
>=75	14	2 (14.3)	12 (85.7)	1.2 (0.9, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9991	0.2253	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.6857
White	176	17 (9.7)	159 (90.3)	12.9 (1.6, NE)	91	8 (8.8)	83 (91.2)	NE (0.8, NE)	0.8165 (0.3478, 1.9169)	0.6505	
Non-White	197	25 (12.7)	172 (87.3)	7.4 (2.7, NE)	92	8 (8.7)	84 (91.3)	NE (1.0, NE)	0.9312 (0.4168, 2.0804)	0.8621	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.3078
Asia	147	18 (12.2)	129 (87.8)	5.7 (1.4, NE)	66	8 (12.1)	58 (87.9)	2.1 (0.7, NE)	0.8143 (0.3490, 1.8999)	0.6312	
North America	60	2 (3.3)	58 (96.7)	NE (4.2, NE)	33	2 (6.1)	31 (93.9)	NE (1.0, NE)	0.2739 (0.0367, 2.0440)	0.1786	
Europe + Israel	166	22 (13.3)	144 (86.7)	7.2 (1.6, NE)	85	6 (7.1)	79 (92.9)	NE (0.8, NE)	1.2657 (0.5111, 3.1343)	0.5899	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	200	19 (9.5)	181 (90.5)	5.6 (1.4, NE)	105	10 (9.5)	95 (90.5)	2.1 (1.0, NE)	0.7040 (0.3217, 1.5409)	0.3759	0.4030
1	173	23 (13.3)	150 (86.7)	7.4 (2.9, NE)	79	6 (7.6)	73 (92.4)	NE (0.8, NE)	1.1571 (0.4695, 2.8517)	0.7436	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.4582
0	60	5 (8.3)	55 (91.7)	7.4 (0.7, NE)	34	2 (5.9)	32 (94.1)	NE (0.7, NE)	0.7311 (0.1390, 3.8465)	0.7710
1	108	17 (15.7)	91 (84.3)	2.9 (1.4, NE)	51	6 (11.8)	45 (88.2)	1.3 (0.7, NE)	0.7718 (0.3033, 1.9643)	0.6052
2	115	11 (9.6)	104 (90.4)	NE (2.9, NE)	54	6 (11.1)	48 (88.9)	2.1 (0.7, NE)	0.5714 (0.2062, 1.5830)	0.2748

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	9 (10.0)	81 (90.0)	9.9 (1.3, NE)	45	2 (4.4)	43 (95.6)	NE (1.2, NE)	1.7359 (0.3543, 8.5051) 0.4964	0.4950

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.0570
PD	174	20 (11.5)	154 (88.5)	9.7 (1.6, NE)	85	5 (5.9)	80 (94.1)	NE (1.2, NE)	1.2751 (0.4744, 3.4273) 0.6300	0.6262	
PR	48	6 (12.5)	42 (87.5)	5.7 (0.7, NE)	22	0	22 (100)	NE (NE, NE)	NE 0.9969	0.1359	
SD	82	8 (9.8)	74 (90.2)	6.7 (0.8, NE)	55	9 (16.4)	46 (83.6)	1.1 (0.7, NE)	0.6497 (0.2473, 1.7073) 0.3817	0.3763	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.0215
Yes	37	3 (8.1)	34 (91.9)	NE (3.0, NE)	15	2 (13.3)	13 (86.7)	1.8 (0.7, NE)	0.0531 (0.0047, 0.5999)	0.0011	
No	336	39 (11.6)	297 (88.4)	6.7 (2.7, 12.5)	169	14 (8.3)	155 (91.7)	NE (1.2, NE)	1.1075 (0.5987, 2.0485)	0.7451	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Baseline CNS metastases											
Yes	24	3 (12.5)	21 (87.5)	NE (1.4, NE)	8	1 (12.5)	7 (87.5)	0.7 (NE, NE)	0.0000 (0.0000, ) 0.9966	0.0027	0.0193
No	349	39 (11.2)	310 (88.8)	6.7 (2.8, 12.9)	176	15 (8.5)	161 (91.5)	NE (1.2, NE)	1.0086 (0.5535, 1.8380) 0.9777	0.9782	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Run date: 10JAN2023 – 19:34; Program name: T3\_EQ5D\_FD\_2\_FAS.sas; Output name: T29BR45.rtf



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## Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.8789
Normal Function	202	23 (11.4)	179 (88.6)	7.4 (2.9, NE)	87	6 (6.9)	81 (93.1)	NE (1.0, NE)	0.8406 (0.3370, 2.0971) 0.7097	0.6972	
Mild Impairment	123	14 (11.4)	109 (88.6)	9.7 (1.6, NE)	69	8 (11.6)	61 (88.4)	NE (0.8, NE)	0.9714 (0.4048, 2.3314) 0.9483	0.9620	
Moderate Impairment	41	5 (12.2)	36 (87.8)	5.7 (0.7, NE)	23	2 (8.7)	21 (91.3)	1.5 (0.7, NE)	0.6831 (0.1314, 3.5506) 0.6504	0.6485	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.9356
Normal Function	170	20 (11.8)	150 (88.2)	5.7 (1.6, NE)	98	9 (9.2)	89 (90.8)	NE (0.8, NE)	0.8826 (0.3955, 1.9696)	0.7572
Mild Impairment	195	22 (11.3)	173 (88.7)	7.4 (2.9, NE)	84	7 (8.3)	77 (91.7)	NE (1.0, NE)	0.8726 (0.3693, 2.0621)	0.7612

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.5314
Yes	332	33 (9.9)	299 (90.1)	9.9 (4.2, NE)	157	14 (8.9)	143 (91.1)	NE (1.2, NE)	0.7874 (0.4185, 1.4812) 0.4584	0.4633	
No	41	9 (22.0)	32 (78.0)	2.1 (0.7, 5.7)	27	2 (7.4)	25 (92.6)	NE (0.7, NE)	1.3520 (0.2915, 6.2703) 0.7000	0.7116	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.8298
Positive	331	39 (11.8)	292 (88.2)	7.2 (2.9, NE)	163	15 (9.2)	148 (90.8)	NE (1.2, NE)	0.8474 (0.4639, 1.5478)	0.5885	
Negative	42	3 (7.1)	39 (92.9)	7.4 (0.7, NE)	21	1 (4.8)	20 (95.2)	NE (0.7, NE)	1.1588 (0.1194, 11.2510)	0.8767	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Hormon receptor status (derived)										0.6528
Positive	333	38 (11.4)	295 (88.6)	9.7 (2.9, NE)	166	15 (9.0)	151 (91.0)	NE (1.2, NE)	0.8349 (0.4559, 1.5290)	0.5575
Negative	40	4 (10.0)	36 (90.0)	7.4 (1.4, NE)	18	1 (5.6)	17 (94.4)	NE (0.7, NE)	1.5466 (0.1717, 13.9280)	0.6951

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

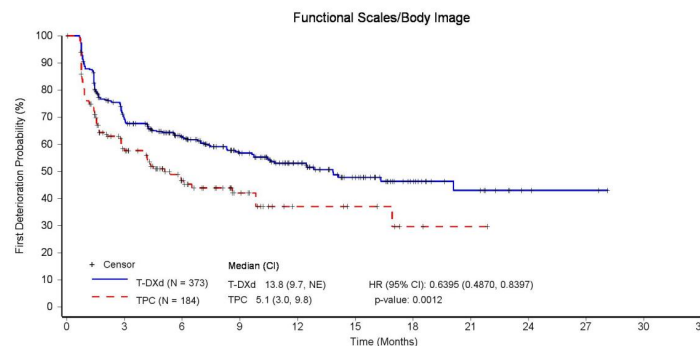
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Run date: 10JAN2023 – 19:34; Program name: T3\_EQ5D\_FD\_2\_FAS.sas; Output name: T29BR45.rtf

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Patients still at risk:

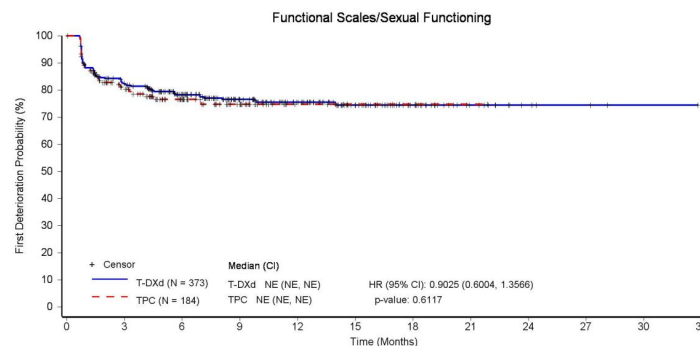
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T-DXd (N = 373)	373	222	162	115	75	44	23	13	3	2	0	0
TPC (N = 184)	184	76	39	20	8	6	2	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

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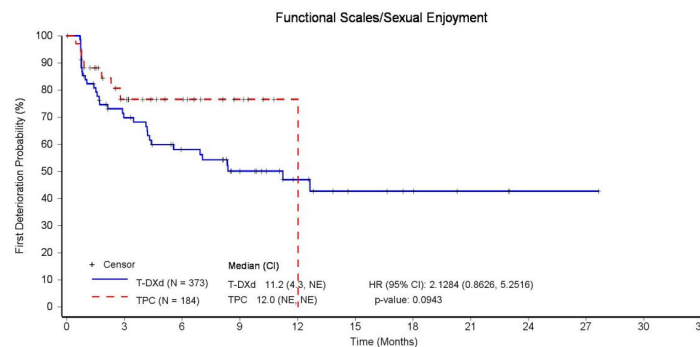
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T-DXd (N = 373)	373	258	200	150	103	63	36	15	5	3	1	0
TPC (N = 184)	184	97	54	29	9	5	2	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	43	31	22	12	7	5	3	1	1	0	0
TPC (N = 184)	184	18	11	5	1	0	0	0	0	0	0	0

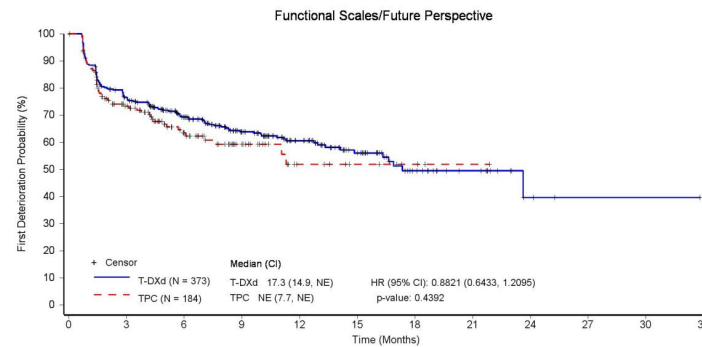
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

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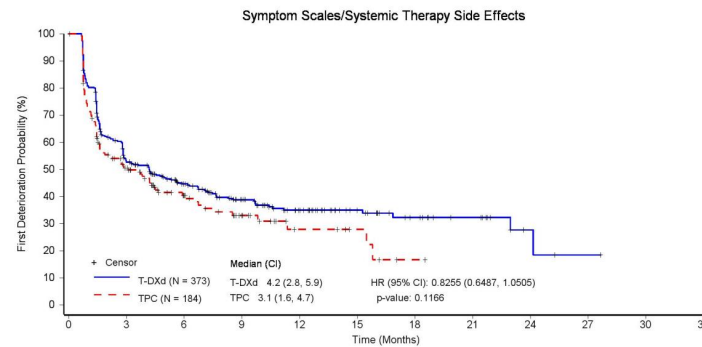
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T-DXd (N = 373)	373	251	188	134	88	52	25	15	3	1	1	0
TPC (N = 184)	184	99	54	26	10	6	3	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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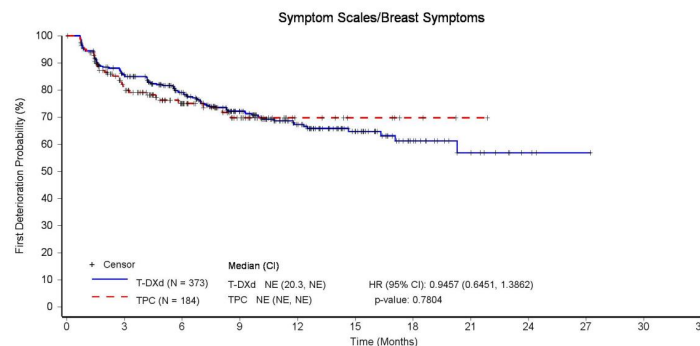
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	171	115	80	51	30	19	12	3	1	0	0
TPC (N = 184)	184	70	36	21	8	5	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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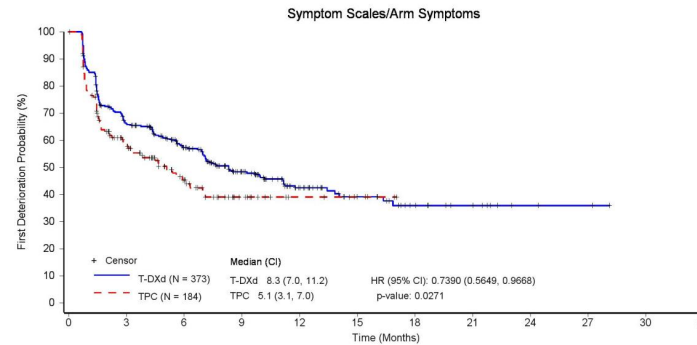
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	271	209	154	96	55	26	12	3	1	0	0
TPC (N = 184)	184	106	58	30	10	6	3	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

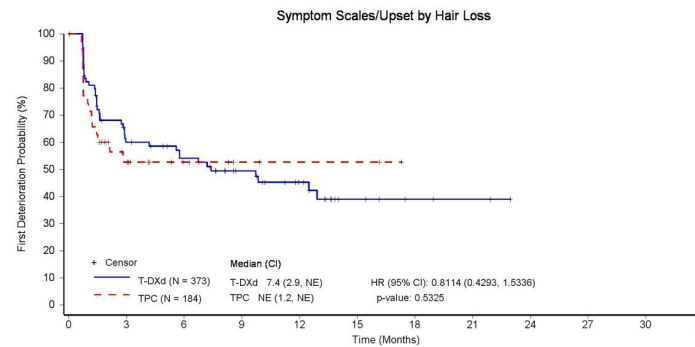
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	214	156	101	54	31	17	10	3	2	0	0
TPC (N = 184)	184	74	34	13	4	2	0	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:34; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F30BR45.rtf

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 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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 DE.F.7.3.3 - EORTC QLQ-BR45 - First deterioration 10 points - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - Full Analysis Set

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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	44	36	24	16	6	3	2	0	0	0	0
TPC (N = 184)	184	14	6	3	2	2	0	0	0	0	0	0

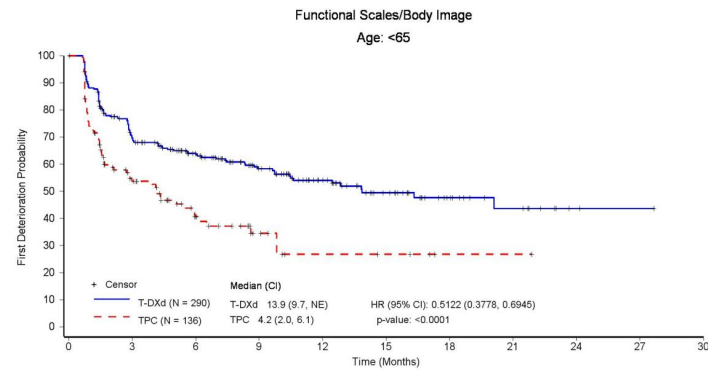
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:34; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F30BR45.rtf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 290)	290	174	128	89	58	35	19	11	2	1	0
TPC (N = 136)	136	51	24	11	5	4	1	1	0	0	0

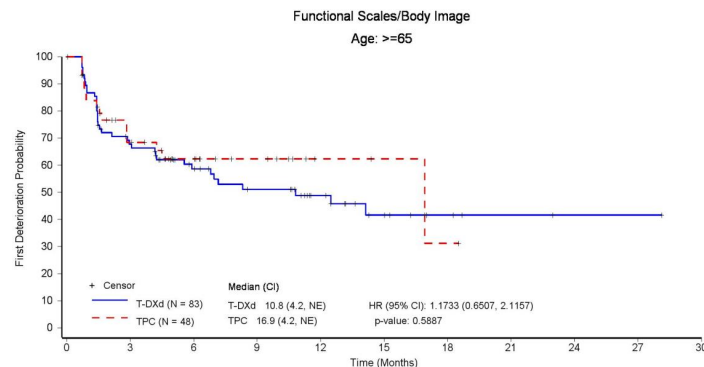
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:35; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F31BR45.rtf

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Patients still at risk:

T-DXd (N = 83)	83	48	34	26	17	9	4	2	1	1	0
TPC (N = 48)	48	25	15	9	3	2	1	0	0	0	0

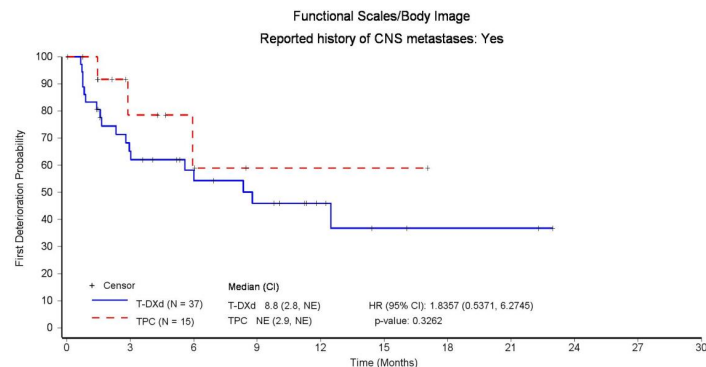
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:35; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F31BR45.rtf

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 11-Jan-2022 - Full Analysis Set



Patients still at risk:

T-DXd (N = 37)	37	21	15	11	6	3	2	2	0	0	0
TPC (N = 15)	15	6	3	1	1	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

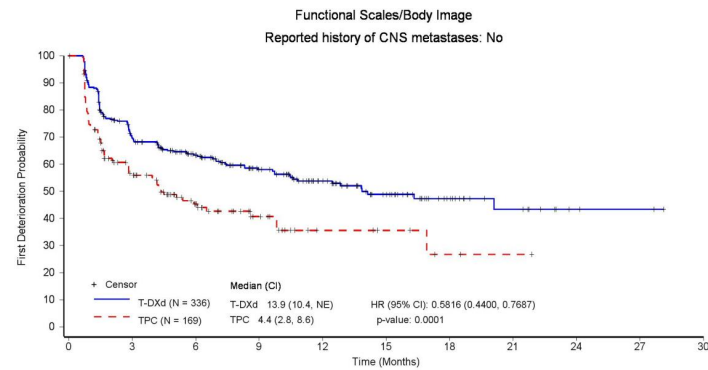
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 Run date: 10JAN2023 – 19:35; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F31BR45.rtf



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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 336)	336	201	147	104	69	41	21	11	3	2	0
TPC (N = 169)	169	70	36	19	7	5	2	1	0	0	0

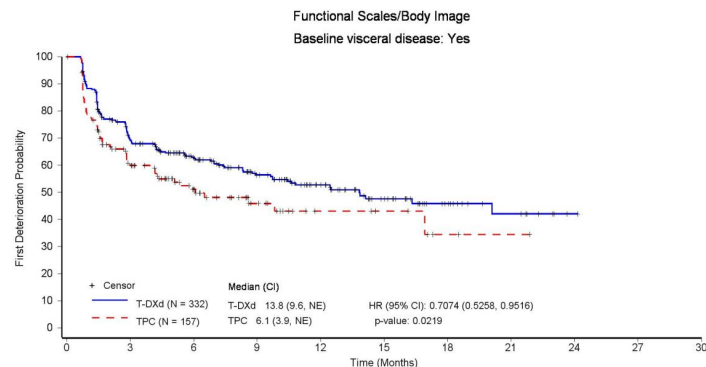
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:35; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F31BR45.rtf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 332)	332	197	143	100	63	37	19	11	1	0	0
TPC (N = 157)	157	68	37	19	8	6	2	1	0	0	0

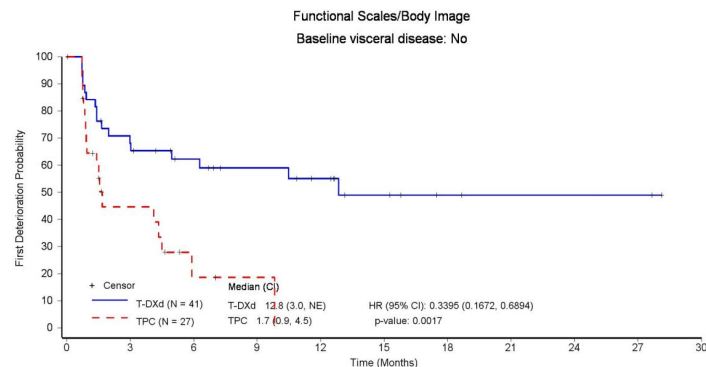
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 11-Jan-2022 - Full Analysis Set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 41)	41	25	19	15	12	7	4	2	2	2	0
TPC (N = 27)	27	8	2	1	0	0	0	0	0	0	0

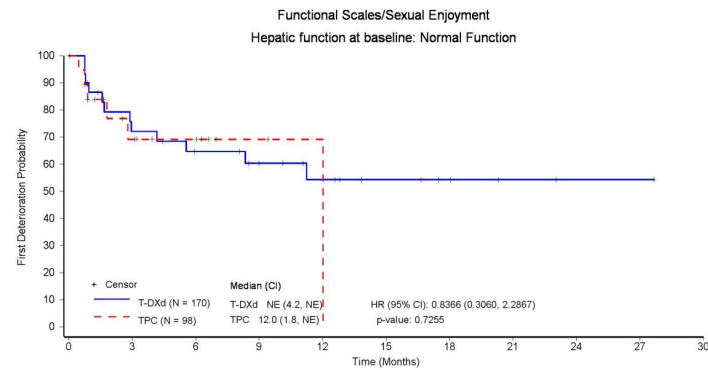
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:35; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F31BR45.rtf

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 11-Jan-2022 - Full Analysis Set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 170)	170	20	16	13	9	6	4	2	1	1	0
TPC (N = 98)	98	9	6	2	1	0	0	0	0	0	0

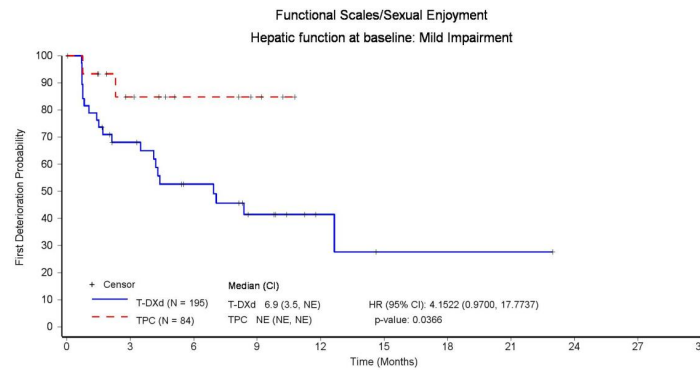
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:35; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F31BR45.rtf

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Patients still at risk:

T-DXd (N = 195)	195	23	15	9	3	1	1	1	0	0	0
TPC (N = 84)	84	9	5	3	0	0	0	0	0	0	0

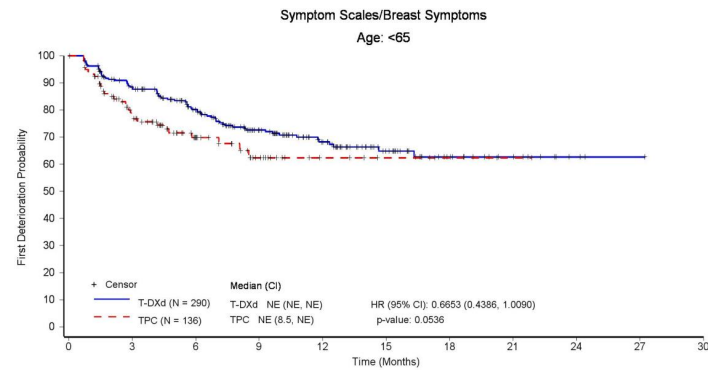
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:35; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F31BR45.rtf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 290)	290	221	168	122	76	41	21	12	3	1	0
TPC (N = 136)	136	73	36	17	7	4	2	1	0	0	0

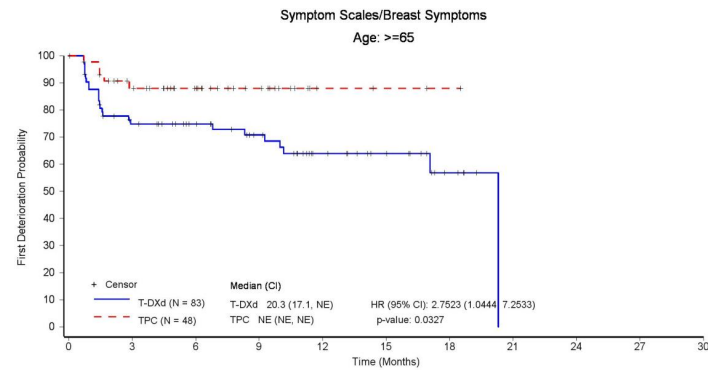
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:35; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F31BR45.rtf

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 11-Jan-2022 - Full Analysis Set



Patients still at risk:

T-DXd (N = 83)	83	50	41	32	20	14	5	0	0	0	0
TPC (N = 48)	48	33	22	13	3	2	1	0	0	0	0

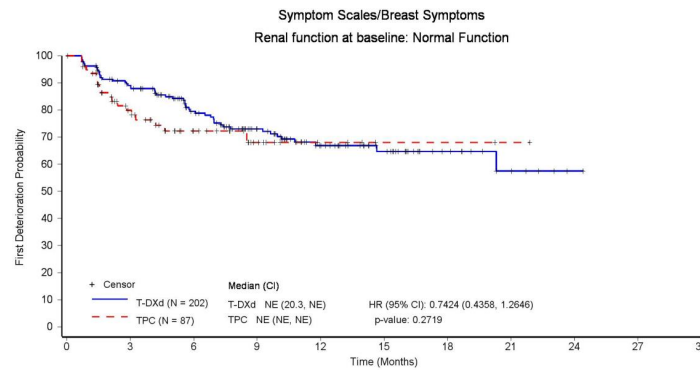
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 202)	202	156	113	82	47	30	14	7	1	0	0
TPC (N = 87)	87	46	23	11	5	2	2	1	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

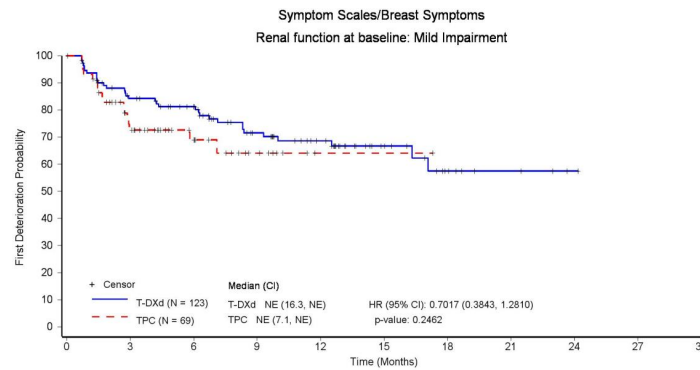
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 123)	123	87	74	52	38	18	8	4	1	0	0
TPC (N = 69)	69	35	19	8	1	1	0	0	0	0	0

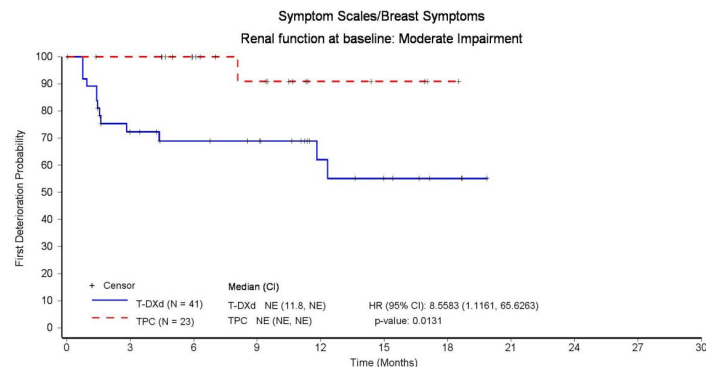
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 41)	41	23	19	17	9	6	3	0	0	0	0
TPC (N = 23)	23	21	14	10	4	3	1	0	0	0	0

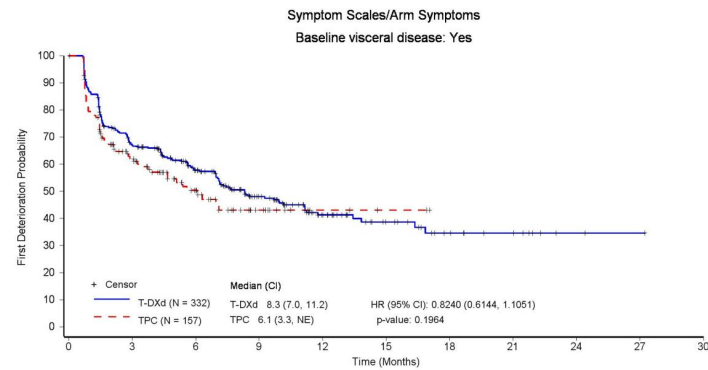
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 11-Jan-2022 - Full Analysis Set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 332)	332	193	138	86	45	24	13	9	2	1	0
TPC (N = 157)	157	68	33	13	4	2	0	0	0	0	0

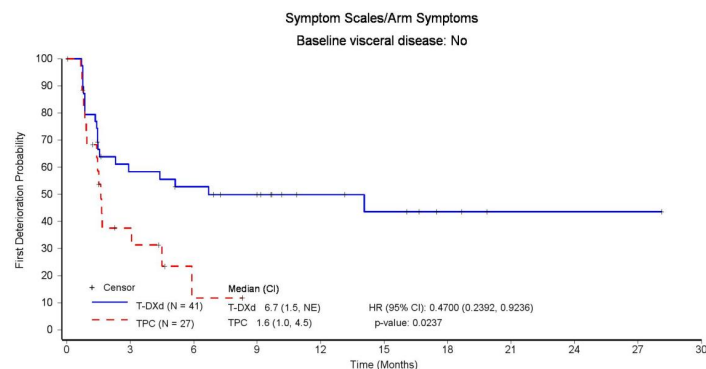
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:35; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F31BR45.rtf

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Patients still at risk:

T-DXd (N = 41)	41	21	18	15	9	7	4	1	1	1	0
TPC (N = 27)	27	6	1	0	0	0	0	0	0	0	0

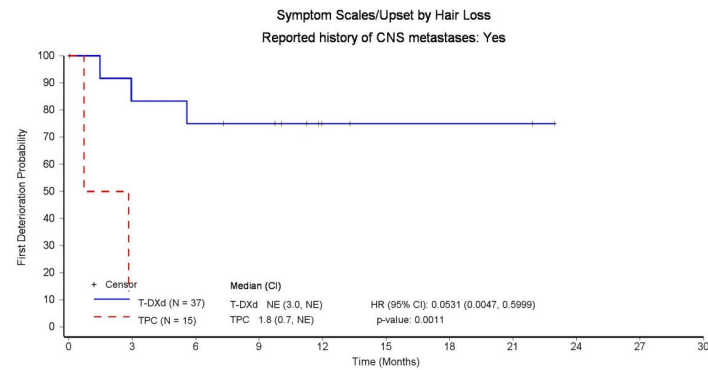
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:35; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F31BR45.rtf

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 11-Jan-2022 - Full Analysis Set



Patients still at risk:

T-DXd (N = 37)	37	10	9	8	3	2	2	2	0	0	0
TPC (N = 15)	15	0	0	0	0	0	0	0	0	0	0

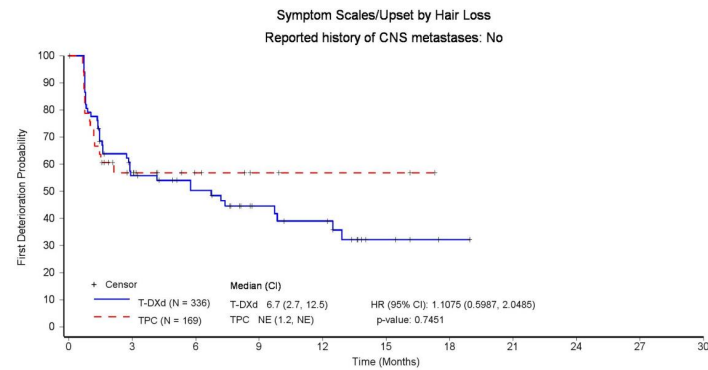
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 11-Jan-2022 - Full Analysis Set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 336)	336	34	27	16	13	4	1	0	0	0	0
TPC (N = 169)	169	14	6	3	2	2	0	0	0	0	0

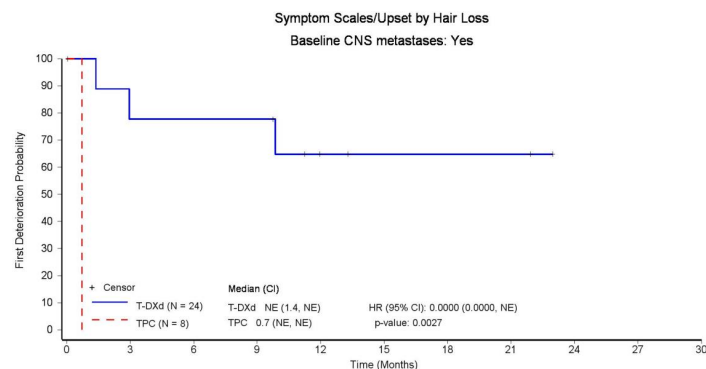
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:35; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F31BR45.rtf

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Patients still at risk:

T-DXd (N = 24)	24	7	7	7	3	2	2	2	0	0	0
TPC (N = 8)	8	0	0	0	0	0	0	0	0	0	0

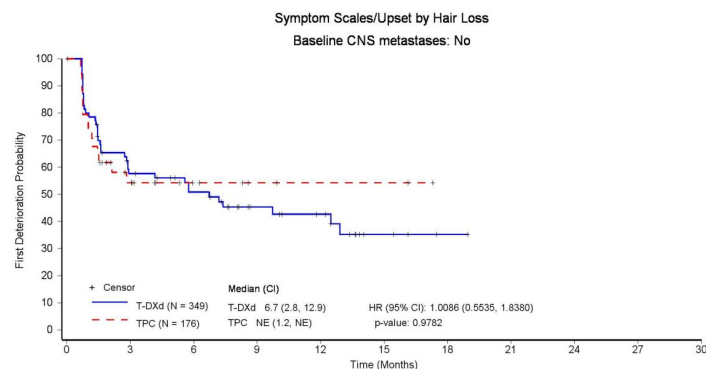
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:35; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F31BR45.rtf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 349)	349	37	29	17	13	4	1	0	0	0	0
TPC (N = 176)	176	14	6	3	2	2	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:35; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F31BR45.rtf



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#### Functional Scales/Body Image

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	116 (31.1)	67 (36.4)	
Number of subjects censored, n (%)	257 (68.9)	117 (63.6)	
Median time to first event (months) [a]	20.1	9.5	
95% Confidence Interval	[16.3, NE]	[5.9, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.5735
95% Confidence Interval			[0.4200, 0.7832]
p-value			0.0005
Stratified log-rank p-value [c]			0.0004

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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#### Functional Scales/Sexual Functioning

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	70 (18.8)	31 (16.8)	
Number of subjects censored, n (%)	303 (81.2)	153 (83.2)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.8321 [0.5411, 1.2795] 0.4024
Stratified log-rank p-value [c]			0.3988

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
Run date: 10JAN2023 – 19:36; Program name: T3\_EQ5D\_FD\_1\_FAS.sas; Output name: T32BR45.rtf

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#### Functional Scales/Sexual Enjoyment

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	21 (5.6)	4 (2.2)	
Number of subjects censored, n (%)	352 (94.4)	180 (97.8)	
Median time to first event (months) [a] 95% Confidence Interval	NE [11.2, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.7769 [0.5847, 5.3993] 0.3107
Stratified log-rank p-value [c]			0.3064

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Run date: 10JAN2023 – 19:36; Program name: T3\_EQ5D\_FD\_1\_FAS.sas; Output name: T32BR45.rtf

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#### Functional Scales/Future Perspective

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	95 (25.5)	44 (23.9)	
Number of subjects censored, n (%)	278 (74.5)	140 (76.1)	
Median time to first event (months) [a] 95% Confidence Interval	NE [20.1, NE]	NE [11.1, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.7659 [0.5308, 1.1051] 0.1539
Stratified log-rank p-value [c]			0.1531

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Symptom Scales/Systemic Therapy Side Effects

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	152 (40.8)	81 (44.0)	
Number of subjects censored, n (%)	221 (59.2)	103 (56.0)	
Median time to first event (months) [a]	15.3	6.7	
95% Confidence Interval	[10.3, NE]	[4.6, 9.8]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.7080
95% Confidence Interval			[0.5371, 0.9334]
p-value			0.0143
Stratified log-rank p-value [c]			0.0132

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Symptom Scales/Breast Symptoms

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	62 (16.6)	23 (12.5)	
Number of subjects censored, n (%)	311 (83.4)	161 (87.5)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.8409 [0.5142, 1.3752] 0.4899
Stratified log-rank p-value [c]			0.4875

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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#### Symptom Scales/Arm Symptoms

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	124 (33.2)	62 (33.7)	
Number of subjects censored, n (%)	249 (66.8)	122 (66.3)	
Median time to first event (months) [a]	18.4	9.1	
95% Confidence Interval	[13.8, NE]	[6.1, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.6127
95% Confidence Interval			[0.4458, 0.8420]
p-value			0.0025
Stratified log-rank p-value [c]			0.0023

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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#### Symptom Scales/Upset by Hair Loss

	T-DXd (N=373)	TPC (N=184)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	32 (8.6)	11 (6.0)	
Number of subjects censored, n (%)	341 (91.4)	173 (94.0)	
Median time to first event (months) [a] 95% Confidence Interval	NE [7.4, NE]	NE [6.0, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.8309 [0.4012, 1.7206] 0.6179
Stratified log-rank p-value [c]			0.6255

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Functional Scales/Body Image

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.8772
HER2 IHC 1+	214	67 (31.3)	147 (68.7)	20.1 (14.1, NE)	107	38 (35.5)	69 (64.5)	9.8 (4.4, NE)	0.5914 (0.3938, 0.8882)	0.0106 (0.0114)
HER2 IHC 2+/ISH Negative	159	49 (30.8)	110 (69.2)	21.9 (14.9, NE)	77	29 (37.7)	48 (62.3)	9.2 (4.5, NE)	0.5362 (0.3340, 0.8609)	0.0086 (0.0099)

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Functional Scales/Body Image

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.1837
1	221	77 (34.8)	144 (65.2)	20.1 (12.8, NE)	100	38 (38.0)	62 (62.0)	14.0 (5.1, NE)	0.6952 (0.4686, 1.0314) 0.0708	0.0689
>=2	151	39 (25.8)	112 (74.2)	21.9 (20.1, NE)	83	29 (34.9)	54 (65.1)	9.5 (4.3, NE)	0.4017 (0.2429, 0.6644) 0.0004	0.0002

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Functional Scales/Body Image

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.4531
Yes	235	70 (29.8)	165 (70.2)	20.1 (20.1, NE)	118	38 (32.2)	80 (67.8)	9.8 (5.9, NE)	0.6580 (0.4405, 0.9830) 0.0410	0.0384	
No	98	34 (34.7)	64 (65.3)	20.1 (12.8, NE)	48	21 (43.8)	27 (56.3)	9.5 (3.9, NE)	0.4730 (0.2692, 0.8311) 0.0092	0.0078	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Age											
<65	290	87 (30.0)	203 (70.0)	20.1 (20.1, NE)	136	56 (41.2)	80 (58.8)	6.1 (4.3, 9.8)	0.4499 (0.3184, 0.6356)	<0.0001	0.0098
>=65	83	29 (34.9)	54 (65.1)	21.9 (10.8, NE)	48	11 (22.9)	37 (77.1)	16.9 (16.9, NE)	1.2253 (0.6054, 2.4801)	0.5722	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7840
<75	359	113 (31.5)	246 (68.5)	20.1 (20.1, NE)	175	63 (36.0)	112 (64.0)	9.2 (5.9, NE)	0.5737 (0.4183, 0.7869) 0.0006	0.0005	
>=75	14	3 (21.4)	11 (78.6)	14.8 (14.1, NE)	9	4 (44.4)	5 (55.6)	16.9 (1.4, NE)	0.4387 (0.0965, 1.9945) 0.2862	0.2735	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.2473
White	176	44 (25.0)	132 (75.0)	NE (20.1, NE)	91	31 (34.1)	60 (65.9)	9.2 (5.1, NE)	0.5132 (0.3209, 0.8207) 0.0054	0.0046	
Non-White	197	72 (36.5)	125 (63.5)	16.3 (12.8, 24.2)	92	35 (38.0)	57 (62.0)	9.8 (4.4, NE)	0.6344 (0.4195, 0.9593) 0.0310	0.0295	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.3073
Asia	147	62 (42.2)	85 (57.8)	14.9 (12.5, 21.9)	66	27 (40.9)	39 (59.1)	9.8 (4.4, NE)	0.6444 (0.4053, 1.0245) 0.0632	0.0610	
North America	60	10 (16.7)	50 (83.3)	NE (10.8, NE)	33	10 (30.3)	23 (69.7)	5.9 (2.9, NE)	0.3254 (0.1304, 0.8120) 0.0161	0.0116	
Europe + Israel	166	44 (26.5)	122 (73.5)	NE (20.1, NE)	85	30 (35.3)	55 (64.7)	9.5 (5.1, NE)	0.5717 (0.3569, 0.9157) 0.0200	0.0181	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.2702
0	200	62 (31.0)	138 (69.0)	20.1 (16.3, NE)	105	39 (37.1)	66 (62.9)	9.5 (4.3, NE)	0.4941 (0.3274, 0.7455) 0.0008	0.0006	
1	173	54 (31.2)	119 (68.8)	21.9 (12.8, NE)	79	28 (35.4)	51 (64.6)	9.2 (5.9, NE)	0.6952 (0.4368, 1.1065) 0.1253	0.1221	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.1284
0	60	21 (35.0)	39 (65.0)	14.8 (8.8, NE)	34	13 (38.2)	21 (61.8)	5.9 (2.9, NE)	0.5855 (0.2845, 1.2050) 0.1461	0.1411
1	108	35 (32.4)	73 (67.6)	20.1 (9.6, NE)	51	18 (35.3)	33 (64.7)	14.0 (5.9, NE)	0.8185 (0.4619, 1.4506) 0.4928	0.4904
2	115	29 (25.2)	86 (74.8)	20.1 (20.1, NE)	54	23 (42.6)	31 (57.4)	5.9 (2.7, NE)	0.3365 (0.1885, 0.6006) 0.0002	0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	31 (34.4)	59 (65.6)	24.2 (12.8, NE)	45	13 (28.9)	32 (71.1)	9.2 (4.4, NE)	0.7074 (0.3619, 1.3829) 0.3115	0.3079

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.5733
PD	174	46 (26.4)	128 (73.6)	20.1 (16.3, NE)	85	27 (31.8)	58 (68.2)	9.8 (5.1, NE)	0.5656 (0.3466, 0.9229) 0.0225	0.0206
PR	48	18 (37.5)	30 (62.5)	14.8 (10.8, NE)	22	9 (40.9)	13 (59.1)	4.3 (1.7, NE)	0.3935 (0.1692, 0.9151) 0.0303	0.0252
SD	82	30 (36.6)	52 (63.4)	21.9 (13.0, NE)	55	20 (36.4)	35 (63.6)	14.0 (5.9, NE)	0.8077 (0.4552, 1.4334) 0.4656	0.4627

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.1780
Yes	37	14 (37.8)	23 (62.2)	21.9 (6.0, NE)	15	3 (20.0)	12 (80.0)	NE (2.9, NE)	1.1434 (0.3218, 4.0628)	0.8386
No	336	102 (30.4)	234 (69.6)	20.1 (16.3, NE)	169	64 (37.9)	105 (62.1)	9.5 (5.9, 16.9)	0.5351 (0.3884, 0.7372)	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.4489
Yes	24	11 (45.8)	13 (54.2)	13.0 (5.8, NE)	8	3 (37.5)	5 (62.5)	5.9 (1.4, NE)	0.7553 (0.2054, 2.7772)	0.6718	
No	349	105 (30.1)	244 (69.9)	20.1 (20.1, NE)	176	64 (36.4)	112 (63.6)	9.5 (5.9, NE)	0.5566 (0.4049, 0.7651)	0.0002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.1521
Normal Function	202	59 (29.2)	143 (70.8)	NE (21.9, NE)	87	36 (41.4)	51 (58.6)	5.9 (3.9, 14.0)	0.4621 (0.3020, 0.7069) 0.0004	0.0003	
Mild Impairment	123	40 (32.5)	83 (67.5)	20.1 (14.1, NE)	69	23 (33.3)	46 (66.7)	NE (4.1, NE)	0.5151 (0.3002, 0.8840) 0.0161	0.0147	
Moderate Impairment	41	13 (31.7)	28 (68.3)	20.1 (11.2, NE)	23	7 (30.4)	16 (69.6)	16.9 (5.9, NE)	1.0946 (0.4300, 2.7860) 0.8496	0.8518	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.6736
Normal Function	170	57 (33.5)	113 (66.5)	21.9 (14.8, NE)	98	40 (40.8)	58 (59.2)	9.5 (4.3, 16.9)	0.5270 (0.3474, 0.7994) 0.0026	0.0021
Mild Impairment	195	57 (29.2)	138 (70.8)	20.1 (14.1, NE)	84	27 (32.1)	57 (67.9)	9.2 (5.1, NE)	0.6031 (0.3780, 0.9622) 0.0339	0.0324

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1111
Yes	332	101 (30.4)	231 (69.6)	20.1 (16.3, NE)	157	51 (32.5)	106 (67.5)	9.8 (8.6, NE)	0.6443 (0.4571, 0.9083) 0.0121	0.0113	
No	41	15 (36.6)	26 (63.4)	NE (9.0, NE)	27	16 (59.3)	11 (40.7)	4.2 (1.7, 5.9)	0.3262 (0.1549, 0.6868) 0.0032	0.0020	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (IXRS)										0.2306
Positive	331	104 (31.4)	227 (68.6)	20.1 (16.3, NE)	163	56 (34.4)	107 (65.6)	9.8 (6.1, NE)	0.6162 (0.4423, 0.8584) 0.0042	0.0038
Negative	42	12 (28.6)	30 (71.4)	21.9 (8.8, NE)	21	11 (52.4)	10 (47.6)	4.2 (1.5, NE)	0.3339 (0.1396, 0.7988) 0.0137	0.0098

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Body Image

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (derived)										0.6184
Positive	333	103 (30.9)	230 (69.1)	20.1 (16.3, NE)	166	59 (35.5)	107 (64.5)	9.5 (6.1, NE)	0.5866 (0.4230, 0.8134) 0.0014	0.0012
Negative	40	13 (32.5)	27 (67.5)	21.9 (8.8, NE)	18	8 (44.4)	10 (55.6)	5.9 (1.4, NE)	0.4443 (0.1764, 1.1188) 0.0851	0.0772

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0700
HER2 IHC 1+	214	41 (19.2)	173 (80.8)	NE (NE, NE)	107	13 (12.1)	94 (87.9)	NE (NE, NE)	1.2322 (0.6556, 2.3159) 0.5167	0.5181	
HER2 IHC 2+/ISH Negative	159	29 (18.2)	130 (81.8)	NE (NE, NE)	77	18 (23.4)	59 (76.6)	NE (NE, NE)	0.5808 (0.3204, 1.0525) 0.0732	0.0698	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.1332
1	221	45 (20.4)	176 (79.6)	NE (NE, NE)	100	14 (14.0)	86 (86.0)	NE (NE, NE)	1.1610 (0.6354, 2.1214) 0.6273	0.6245
>=2	151	25 (16.6)	126 (83.4)	NE (20.0, NE)	83	17 (20.5)	66 (79.5)	NE (NE, NE)	0.5925 (0.3146, 1.1157) 0.1050	0.1011

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.1498
Yes	235	43 (18.3)	192 (81.7)	NE (NE, NE)	118	22 (18.6)	96 (81.4)	NE (NE, NE)	0.6954 (0.4128, 1.1716) 0.1723	0.1695	
No	98	20 (20.4)	78 (79.6)	NE (NE, NE)	48	5 (10.4)	43 (89.6)	NE (NE, NE)	1.6759 (0.6251, 4.4930) 0.3048	0.3000	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0836
<65	290	58 (20.0)	232 (80.0)	NE (NE, NE)	136	28 (20.6)	108 (79.4)	NE (NE, NE)	0.6933 (0.4389, 1.0953) 0.1165	0.1136	
>=65	83	12 (14.5)	71 (85.5)	NE (20.0, NE)	48	3 (6.3)	45 (93.8)	NE (NE, NE)	2.1193 (0.5912, 7.5976) 0.2489	0.2382	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Age											
<75	359	69 (19.2)	290 (80.8)	NE (NE, NE)	175	30 (17.1)	145 (82.9)	NE (NE, NE)	0.8357 (0.5415, 1.2898)	0.4153	0.9803
>=75	14	1 (7.1)	13 (92.9)	NE (NE, NE)	9	1 (11.1)	8 (88.9)	NE (0.7, NE)	0.7071 (0.0442, 11.3185)	0.8055	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.0454
White	176	38 (21.6)	138 (78.4)	NE (20.0, NE)	91	22 (24.2)	69 (75.8)	NE (8.1, NE)	0.5972 (0.3494, 1.0207) 0.0594	0.0571	
Non-White	197	32 (16.2)	165 (83.8)	NE (NE, NE)	92	8 (8.7)	84 (91.3)	NE (NE, NE)	1.5883 (0.7289, 3.4610) 0.2444	0.2376	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.3052
Asia	147	21 (14.3)	126 (85.7)	NE (NE, NE)	66	5 (7.6)	61 (92.4)	NE (NE, NE)	1.5704 (0.5883, 4.1919) 0.3676	0.3587	
North America	60	8 (13.3)	52 (86.7)	NE (NE, NE)	33	6 (18.2)	27 (81.8)	NE (4.5, NE)	0.5694 (0.1957, 1.6561) 0.3012	0.2933	
Europe + Israel	166	41 (24.7)	125 (75.3)	NE (20.0, NE)	85	20 (23.5)	65 (76.5)	NE (NE, NE)	0.7595 (0.4413, 1.3073) 0.3207	0.3205	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
ECOG PS										0.7423
0	200	43 (21.5)	157 (78.5)	NE (NE, NE)	105	20 (19.0)	85 (81.0)	NE (NE, NE)	0.7972 (0.4658, 1.3644)	0.4128
1	173	27 (15.6)	146 (84.4)	NE (NE, NE)	79	11 (13.9)	68 (86.1)	NE (NE, NE)	0.9852 (0.4873, 1.9919)	0.9626

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.1046
0	60	11 (18.3)	49 (81.7)	NE (NE, NE)	34	8 (23.5)	26 (76.5)	NE (3.4, NE)	0.5937 (0.2376, 1.4838)	0.2601
1	108	24 (22.2)	84 (77.8)	NE (18.6, NE)	51	5 (9.8)	46 (90.2)	NE (NE, NE)	2.0151 (0.7645, 5.3118)	0.1484
2	115	22 (19.1)	93 (80.9)	NE (NE, NE)	54	9 (16.7)	45 (83.3)	NE (8.1, NE)	0.8259 (0.3757, 1.8157)	0.6261

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	13 (14.4)	77 (85.6)	NE (NE, NE)	45	9 (20.0)	36 (80.0)	NE (NE, NE)	0.5114 (0.2157, 1.2127) 0.1280	0.1204

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.1555
PD	174	39 (22.4)	135 (77.6)	NE (18.6, NE)	85	17 (20.0)	68 (80.0)	NE (NE, NE)	0.8134 (0.4565, 1.4492) 0.4834	0.4825	
PR	48	4 (8.3)	44 (91.7)	NE (NE, NE)	22	4 (18.2)	18 (81.8)	NE (3.1, NE)	0.2264 (0.0545, 0.9394) 0.0408	0.0263	
SD	82	14 (17.1)	68 (82.9)	NE (20.0, NE)	55	6 (10.9)	49 (89.1)	NE (NE, NE)	1.3572 (0.5170, 3.5630) 0.5351	0.5343	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.4704
Yes	37	7 (18.9)	30 (81.1)	NE (NE, NE)	15	3 (20.0)	12 (80.0)	NE (0.9, NE)	0.4753 (0.1150, 1.9642) 0.3042	0.2948
No	336	63 (18.8)	273 (81.3)	NE (NE, NE)	169	28 (16.6)	141 (83.4)	NE (NE, NE)	0.8934 (0.5697, 1.4008) 0.6232	0.6226

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.4819
Yes	24	4 (16.7)	20 (83.3)	NE (NE, NE)	8	2 (25.0)	6 (75.0)	NE (0.9, NE)	0.3406 (0.0538, 2.1544)	0.2312
No	349	66 (18.9)	283 (81.1)	NE (NE, NE)	176	29 (16.5)	147 (83.5)	NE (NE, NE)	0.8945 (0.5755, 1.3902)	0.6200

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.3418
Normal Function	202	40 (19.8)	162 (80.2)	NE (NE, NE)	87	19 (21.8)	68 (78.2)	NE (NE, NE)	0.6492 (0.3736, 1.1282) 0.1255	0.1215	
Mild Impairment	123	26 (21.1)	97 (78.9)	NE (20.0, NE)	69	9 (13.0)	60 (87.0)	NE (NE, NE)	1.1658 (0.5390, 2.5218) 0.6967	0.6975	
Moderate Impairment	41	4 (9.8)	37 (90.2)	NE (NE, NE)	23	2 (8.7)	21 (91.3)	NE (NE, NE)	1.2821 (0.2344, 7.0136) 0.7744	0.7739	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.4437
Normal Function	170	35 (20.6)	135 (79.4)	NE (NE, NE)	98	21 (21.4)	77 (78.6)	NE (NE, NE)	0.7748 (0.4491, 1.3369)	0.3556	
Mild Impairment	195	35 (17.9)	160 (82.1)	NE (20.0, NE)	84	10 (11.9)	74 (88.1)	NE (NE, NE)	1.0584 (0.5191, 2.1583)	0.8734	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.8431
Yes	332	58 (17.5)	274 (82.5)	NE (NE, NE)	157	24 (15.3)	133 (84.7)	NE (NE, NE)	0.8483 (0.5243, 1.3725) 0.5027	0.5016	
No	41	12 (29.3)	29 (70.7)	NE (6.9, NE)	27	7 (25.9)	20 (74.1)	NE (4.5, NE)	1.0491 (0.4118, 2.6723) 0.9200	0.9227	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.5550
Positive	331	63 (19.0)	268 (81.0)	NE (NE, NE)	163	26 (16.0)	137 (84.0)	NE (NE, NE)	0.8980 (0.5659, 1.4249)	0.6478	0.6468
Negative	42	7 (16.7)	35 (83.3)	NE (NE, NE)	21	5 (23.8)	16 (76.2)	NE (3.4, NE)	0.6219 (0.1943, 1.9904)	0.4199	0.4236

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Functioning

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.6594
Positive	333	63 (18.9)	270 (81.1)	NE (NE, NE)	166	27 (16.3)	139 (83.7)	NE (NE, NE)	0.8921 (0.5658, 1.4066)	0.6213	
Negative	40	7 (17.5)	33 (82.5)	NE (10.6, NE)	18	4 (22.2)	14 (77.8)	NE (1.6, NE)	0.5557 (0.1543, 2.0019)	0.3634	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.0054
HER2 IHC 1+	214	9 (4.2)	205 (95.8)	NE (10.9, NE)	107	4 (3.7)	103 (96.3)	NE (0.9, NE)	0.6410 (0.1869, 2.1981)	0.4819
HER2 IHC 2+/ISH Negative	159	12 (7.5)	147 (92.5)	NE (7.1, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE)	0.0240

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.3640
1	221	11 (5.0)	210 (95.0)	NE (11.2, NE)	100	3 (3.0)	97 (97.0)	NE (NE, NE)	1.3592 (0.3745, 4.9327) 0.6407	0.6304
>=2	151	10 (6.6)	141 (93.4)	NE (4.1, NE)	83	1 (1.2)	82 (98.8)	NE (NE, NE)	3.8462 (0.4827, 30.6437) 0.2033	0.1713

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.9379
Yes	235	14 (6.0)	221 (94.0)	NE (NE, NE)	118	2 (1.7)	116 (98.3)	NE (NE, NE)	2.3340 (0.5262, 10.3527) 0.2648	0.2493	
No	98	5 (5.1)	93 (94.9)	NE (1.7, NE)	48	1 (2.1)	47 (97.9)	NE (0.8, NE)	2.0777 (0.2386, 18.0902) 0.5078	0.4904	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5973
<65	290	18 (6.2)	272 (93.8)	NE (11.2, NE)	136	3 (2.2)	133 (97.8)	NE (NE, NE)	2.2420 (0.6527, 7.7015) 0.1997	0.1871	
>=65	83	3 (3.6)	80 (96.4)	NE (2.1, NE)	48	1 (2.1)	47 (97.9)	NE (0.8, NE)	0.7944 (0.0702, 8.9933) 0.8525	0.8522	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											
<75	359	21 (5.8)	338 (94.2)	NE (11.2, NE)	175	4 (2.3)	171 (97.7)	NE (NE, NE)	1.9870 (0.6742, 5.8561) 0.2131	0.2014	NE
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Race										0.0614
White	176	12 (6.8)	164 (93.2)	NE (8.8, NE)	91	1 (1.1)	90 (98.9)	NE (NE, NE)	5.2332 (0.6763, 40.4921) 0.1129	0.0769
Non-White	197	9 (4.6)	188 (95.4)	NE (10.9, NE)	92	3 (3.3)	89 (96.7)	NE (0.8, NE)	0.6952 (0.1862, 2.5948) 0.5885	0.6076

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.1656
Asia	147	5 (3.4)	142 (96.6)	11.2 (0.8, NE)	66	0	66 (100)	NE (NE, NE)	NE (NE, NE) 0.9972	0.2248	
North America	60	5 (8.3)	55 (91.7)	NE (2.1, NE)	33	0	33 (100)	NE (NE, NE)	NE (NE, NE) 0.9960	0.2710	
Europe + Israel	166	11 (6.6)	155 (93.4)	NE (NE, NE)	85	4 (4.7)	81 (95.3)	NE (NE, NE)	1.2172 (0.3830, 3.8679) 0.7390	0.7324	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.8061
0	200	12 (6.0)	188 (94.0)	NE (8.8, NE)	105	3 (2.9)	102 (97.1)	NE (NE, NE)	1.7839 (0.4946, 6.4347) 0.3765	0.3641	
1	173	9 (5.2)	164 (94.8)	NE (6.9, NE)	79	1 (1.3)	78 (98.7)	NE (NE, NE)	2.4851 (0.3083, 20.0327) 0.3926	0.3775	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1532
0	60	4 (6.7)	56 (93.3)	10.9 (1.1, NE)	34	1 (2.9)	33 (97.1)	NE (0.9, NE)	2.3033 (0.2567, 20.6683) 0.4561	0.4432	
1	108	7 (6.5)	101 (93.5)	NE (4.3, NE)	51	3 (5.9)	48 (94.1)	NE (0.8, NE)	0.7781 (0.2004, 3.0209) 0.7170	0.7445	
2	115	7 (6.1)	108 (93.9)	NE (8.8, NE)	54	0	54 (100)	NE (NE, NE)	NE (NE, NE) 0.9951	0.1626	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	3 (3.3)	87 (96.7)	NE (3.6, NE)	45	0	45 (100)	NE (NE, NE)	NE (NE, NE) 0.9968	0.2994	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.1623
PD	174	10 (5.7)	164 (94.3)	NE (10.9, NE)	85	3 (3.5)	82 (96.5)	NE (NE, NE)	1.4273 (0.3841, 5.3034) 0.5953	0.5921	
PR	48	2 (4.2)	46 (95.8)	NE (0.8, NE)	22	0	22 (100)	NE (NE, NE)	NE (NE, NE) 0.9979	0.2649	
SD	82	6 (7.3)	76 (92.7)	NE (2.1, NE)	55	0	55 (100)	NE (NE, NE)	NE (NE, NE) 0.9965	0.0900	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.3733
Yes	37	3 (8.1)	34 (91.9)	NE (1.6, NE)	15	0	15 (100)	NE (NE, NE)	NE (NE, NE) 0.9975	0.5017	
No	336	18 (5.4)	318 (94.6)	NE (11.2, NE)	169	4 (2.4)	165 (97.6)	NE (NE, NE)	1.7618 (0.5881, 5.2779) 0.3117	0.3012	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											NE
Yes	24	1 (4.2)	23 (95.8)	NE (1.6, NE)	8	0	8 (100)	NE (NE, NE)	NE (NE, NE)		
No	349	20 (5.7)	329 (94.3)	NE (11.2, NE)	176	4 (2.3)	172 (97.7)	NE (NE, NE)	1.9217 (0.6483, 5.6964)	0.2274	0.2387

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.3203
Normal Function	202	15 (7.4)	187 (92.6)	NE (7.1, NE)	87	3 (3.4)	84 (96.6)	NE (NE, NE)	1.6545 (0.4744, 5.7708) 0.4296	0.4234	
Mild Impairment	123	4 (3.3)	119 (96.7)	NE (8.8, NE)	69	0	69 (100)	NE (NE, NE)	NE (NE, NE) 0.9959	0.2215	
Moderate Impairment	41	2 (4.9)	39 (95.1)	11.2 (1.6, NE)	23	1 (4.3)	22 (95.7)	NE (0.8, NE)	0.4714 (0.0283, 7.8580) 0.6004	0.5924	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.1086
Normal Function	170	6 (3.5)	164 (96.5)	NE (NE, NE)	98	3 (3.1)	95 (96.9)	NE (NE, NE)	0.9244 (0.2246, 3.8050)	0.9144
Mild Impairment	195	15 (7.7)	180 (92.3)	NE (6.9, NE)	84	1 (1.2)	83 (98.8)	NE (NE, NE)	5.0197 (0.6591, 38.2290)	0.0819

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.3432
Yes	332	17 (5.1)	315 (94.9)	NE (NE, NE)	157	3 (1.9)	154 (98.1)	NE (NE, NE)	2.6345 (0.7702, 9.0117)	0.1058	
No	41	4 (9.8)	37 (90.2)	NE (8.8, NE)	27	1 (3.7)	26 (96.3)	NE (0.9, NE)	0.1818 (0.0096, 3.4390)	0.2126	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (IXRS)										0.8257
Positive	331	18 (5.4)	313 (94.6)	NE (NE, NE)	163	3 (1.8)	160 (98.2)	NE (NE, NE)	2.1230 (0.6198, 7.2719)	0.2158
Negative	42	3 (7.1)	39 (92.9)	6.2 (1.1, NE)	21	1 (4.8)	20 (95.2)	NE (0.9, NE)	1.8227 (0.1645, 20.1957)	0.6195

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Sexual Enjoyment

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.8938
Positive	333	19 (5.7)	314 (94.3)	NE (NE, NE)	166	3 (1.8)	163 (98.2)	NE (NE, NE)	2.2707 (0.6666, 7.7349) 0.1897	0.1741	
Negative	40	2 (5.0)	38 (95.0)	10.9 (1.1, NE)	18	1 (5.6)	17 (94.4)	NE (0.9, NE)	0.8165 (0.0503, 13.2411) 0.8866	0.8864	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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[c] Two-sided p-value from unstratified log-rank test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.3009
HER2 IHC 1+	214	55 (25.7)	159 (74.3)	NE (17.3, NE)	107	22 (20.6)	85 (79.4)	NE (11.1, NE)	0.8451 (0.5097, 1.4012)	0.5134
HER2 IHC 2+/ISH Negative	159	40 (25.2)	119 (74.8)	NE (NE, NE)	77	22 (28.6)	55 (71.4)	NE (6.1, NE)	0.6171 (0.3637, 1.0468)	0.0716

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.0644
1	221	60 (27.1)	161 (72.9)	NE (17.3, NE)	100	21 (21.0)	79 (79.0)	NE (10.7, NE)	0.9984 (0.6034, 1.6519) 0.9949	0.9964
>=2	151	35 (23.2)	116 (76.8)	NE (NE, NE)	83	23 (27.7)	60 (72.3)	NE (5.9, NE)	0.5019 (0.2928, 0.8602) 0.0122	0.0106

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.2806
Yes	235	61 (26.0)	174 (74.0)	NE (17.3, NE)	118	24 (20.3)	94 (79.7)	NE (10.7, NE)	0.8683 (0.5371, 1.4038) 0.5645	0.5661	
No	98	25 (25.5)	73 (74.5)	NE (16.6, NE)	48	15 (31.3)	33 (68.8)	NE (7.1, NE)	0.5635 (0.2927, 1.0849) 0.0861	0.0820	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Age										0.2393
<65	290	65 (22.4)	225 (77.6)	NE (NE, NE)	136	30 (22.1)	106 (77.9)	NE (NE, NE)	0.6857 (0.4417, 1.0644) 0.0926	0.0914
>=65	83	30 (36.1)	53 (63.9)	17.3 (10.0, NE)	48	14 (29.2)	34 (70.8)	11.3 (10.7, NE)	0.9806 (0.5142, 1.8703) 0.9526	0.9529

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Age											
<75	359	89 (24.8)	270 (75.2)	NE (20.1, NE)	175	41 (23.4)	134 (76.6)	NE (10.7, NE)	0.7231 (0.4963, 1.0535) 0.0913	0.0905	0.2513
>=75	14	6 (42.9)	8 (57.1)	14.1 (4.2, NE)	9	3 (33.3)	6 (66.7)	11.3 (3.8, NE)	1.3976 (0.3454, 5.6551) 0.6388	0.6372	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Race										0.5019
White	176	31 (17.6)	145 (82.4)	NE (NE, NE)	91	17 (18.7)	74 (81.3)	NE (11.1, NE)	0.6636 (0.3627, 1.2140) 0.1833	0.1808
Non-White	197	64 (32.5)	133 (67.5)	20.1 (16.6, NE)	92	27 (29.3)	65 (70.7)	11.3 (9.0, NE)	0.7816 (0.4952, 1.2336) 0.2899	0.2889

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Region										0.1654
Asia	147	46 (31.3)	101 (68.7)	NE (17.3, NE)	66	24 (36.4)	42 (63.6)	10.7 (6.1, NE)	0.6048 (0.3665, 0.9978) 0.0490	0.0472
North America	60	9 (15.0)	51 (85.0)	NE (NE, NE)	33	7 (21.2)	26 (78.8)	NE (2.1, NE)	0.5659 (0.2086, 1.5353) 0.2635	0.2585
Europe + Israel	166	40 (24.1)	126 (75.9)	NE (17.3, NE)	85	13 (15.3)	72 (84.7)	NE (11.1, NE)	1.1130 (0.5904, 2.0984) 0.7407	0.7409

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	200	55 (27.5)	145 (72.5)	NE (17.3, NE)	105	27 (25.7)	78 (74.3)	NE (9.0, NE)	0.6562 (0.4103, 1.0494)	0.0784	0.4672
1	173	40 (23.1)	133 (76.9)	NE (NE, NE)	79	17 (21.5)	62 (78.5)	NE (11.3, NE)	0.8981 (0.5062, 1.5934)	0.7093	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)									0.4606
0	60	18 (30.0)	42 (70.0) (13.9, NE)	34	9 (26.5)	25 (73.5) (5.9, NE)	0.8256 (0.3669, 1.8575) 0.6432	0.6367	
1	108	21 (19.4)	87 (80.6) (17.3, NE)	51	12 (23.5)	39 (76.5) (11.1, NE)	0.6628 (0.3245, 1.3537) 0.2590	0.2557	
2	115	29 (25.2)	86 (74.8) (17.3, NE)	54	15 (27.8)	39 (72.2) (5.1, NE)	0.4897 (0.2538, 0.9448) 0.0332	0.0299	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	27 (30.0)	63 (70.0)	NE (16.3, NE)	45	8 (17.8)	37 (82.2)	NE (NE, NE)	1.2639 (0.5696, 2.8043) 0.5647	0.5627	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.4130
PD	174	46 (26.4)	128 (73.6)	20.1 (16.3, NE)	85	15 (17.6)	70 (82.4)	NE (10.7, NE)	1.0153 (0.5610, 1.8375) 0.9599	0.9563	
PR	48	15 (31.3)	33 (68.8)	NE (11.2, NE)	22	7 (31.8)	15 (68.2)	9.0 (3.8, NE)	0.4881 (0.1940, 1.2283) 0.1277	0.1196	
SD	82	21 (25.6)	61 (74.4)	NE (NE, NE)	55	15 (27.3)	40 (72.7)	11.3 (11.1, NE)	0.6992 (0.3563, 1.3721) 0.2982	0.2937	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.5353
Yes	37	7 (18.9)	30 (81.1)	NE (NE, NE)	15	3 (20.0)	12 (80.0)	NE (2.1, NE)	0.5019 (0.1235, 2.0396)	0.3275
No	336	88 (26.2)	248 (73.8)	NE (20.1, NE)	169	41 (24.3)	128 (75.7)	NE (10.7, NE)	0.7626 (0.5230, 1.1120)	0.1580

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.6998
Yes	24	5 (20.8)	19 (79.2)	NE (NE, NE)	8	1 (12.5)	7 (87.5)	NE (4.3, NE)	1.0990 (0.1240, 9.7391) 0.9324	0.9324	
No	349	90 (25.8)	259 (74.2)	NE (20.1, NE)	176	43 (24.4)	133 (75.6)	NE (10.7, NE)	0.7368 (0.5090, 1.0664) 0.1054	0.1044	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.6501
Normal Function	202	45 (22.3)	157 (77.7)	NE (NE, NE)	87	17 (19.5)	70 (80.5)	NE (NE, NE)	0.7864 (0.4462, 1.3860) 0.4060	0.4084	
Mild Impairment	123	36 (29.3)	87 (70.7)	20.1 (14.9, NE)	69	20 (29.0)	49 (71.0)	NE (5.9, NE)	0.6282 (0.3571, 1.1048) 0.1065	0.1048	
Moderate Impairment	41	13 (31.7)	28 (68.3)	NE (11.2, NE)	23	7 (30.4)	16 (69.6)	11.3 (7.7, NE)	1.0176 (0.4050, 2.5571) 0.9704	0.9726	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.8575
Normal Function	170	43 (25.3)	127 (74.7)	NE (20.1, NE)	98	24 (24.5)	74 (75.5)	NE (9.0, NE)	0.6847 (0.4114, 1.1396) 0.1451	0.1418
Mild Impairment	195	51 (26.2)	144 (73.8)	NE (17.3, NE)	84	20 (23.8)	64 (76.2)	11.3 (10.7, NE)	0.7687 (0.4543, 1.3008) 0.3271	0.3272

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline visceral disease										0.7868
Yes	332	85 (25.6)	247 (74.4)	NE (20.1, NE)	157	39 (24.8)	118 (75.2)	NE (11.1, NE)	0.7218 (0.4912, 1.0607) 0.0969	0.0963
No	41	10 (24.4)	31 (75.6)	NE (NE, NE)	27	5 (18.5)	22 (81.5)	9.0 (5.9, NE)	0.9173 (0.3091, 2.7219) 0.8764	0.8745

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (IXRS)										0.9789
Positive	331	85 (25.7)	246 (74.3)	NE (20.1, NE)	163	39 (23.9)	124 (76.1)	NE (11.1, NE)	0.7359 (0.5005, 1.0819) 0.1188	0.1180
Negative	42	10 (23.8)	32 (76.2)	NE (NE, NE)	21	5 (23.8)	16 (76.2)	9.0 (4.5, NE)	0.8185 (0.2772, 2.4164) 0.7168	0.7103

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Functional Scales/Future Perspective

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (derived)										0.7794
Positive	333	85 (25.5)	248 (74.5)	NE (20.1, NE)	166	39 (23.5)	127 (76.5)	NE (11.1, NE)	0.7470 (0.5079, 1.0985)	0.1375
Negative	40	10 (25.0)	30 (75.0)	NE (NE, NE)	18	5 (27.8)	13 (72.2)	9.0 (4.5, NE)	0.7151 (0.2428, 2.1060)	0.5351

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.6043
HER2 IHC 1+	214	84 (39.3)	130 (60.7)	15.3 (10.4, NE)	107	47 (43.9)	60 (56.1)	7.0 (4.4, 9.8)	0.6437 (0.4480, 0.9249) 0.0172	0.0163
HER2 IHC 2+/ISH Negative	159	68 (42.8)	91 (57.2)	22.3 (6.9, NE)	77	34 (44.2)	43 (55.8)	6.1 (4.3, NE)	0.7791 (0.5140, 1.1809) 0.2394	0.2318

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[c] Two-sided p-value from unstratified log-rank test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.5737
1	221	95 (43.0)	126 (57.0)	14.1 (7.8, NE)	100	47 (47.0)	53 (53.0)	6.7 (4.5, 11.4)	0.7503 (0.5275, 1.0674)	0.1059
>=2	151	56 (37.1)	95 (62.9)	23.0 (10.4, NE)	83	34 (41.0)	49 (59.0)	6.1 (3.9, NE)	0.6299 (0.4080, 0.9725)	0.0346

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[c] Two-sided p-value from unstratified log-rank test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.4703
Yes	235	99 (42.1)	136 (57.9)	14.1 (7.6, 23.0)	118	53 (44.9)	65 (55.1)	6.7 (4.4, 8.5)	0.6955 (0.4957, 0.9759) 0.0356	0.0332	
No	98	38 (38.8)	60 (61.2)	NE (10.4, NE)	48	23 (47.9)	25 (52.1)	5.9 (2.1, NE)	0.5889 (0.3489, 0.9939) 0.0474	0.0458	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3544
<65	290	116 (40.0)	174 (60.0)	16.3 (10.4, NE)	136	59 (43.4)	77 (56.6)	5.9 (4.3, 9.8)	0.6459 (0.4694, 0.8889) 0.0073	0.0066	
>=65	83	36 (43.4)	47 (56.6)	11.2 (4.6, NE)	48	22 (45.8)	26 (54.2)	7.0 (4.5, NE)	0.9136 (0.5367, 1.5554) 0.7393	0.7458	

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[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Age										0.0142
<75	359	143 (39.8)	216 (60.2)	16.3 (10.9, NE)	175	78 (44.6)	97 (55.4)	6.1 (4.5, 8.5)	0.6474 (0.4891, 0.8568)	0.0024
>=75	14	9 (64.3)	5 (35.7)	4.2 (1.4, 14.1)	9	3 (33.3)	6 (66.7)	NE (1.6, NE)	3.2570 (0.8707, 12.1839)	0.0625

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Race										0.2144
White	176	74 (42.0)	102 (58.0)	14.1 (6.9, NE)	91	35 (38.5)	56 (61.5)	7.7 (4.5, NE)	0.8431 (0.5616, 1.2658)	0.4042
Non-White	197	78 (39.6)	119 (60.4)	23.0 (10.9, NE)	92	46 (50.0)	46 (50.0)	6.1 (4.2, 8.5)	0.5908 (0.4082, 0.8550)	0.0046

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.7772
Asia	147	65 (44.2)	82 (55.8)	16.3 (7.6, NE)	66	35 (53.0)	31 (47.0)	6.1 (4.2, 9.8)	0.6446 (0.4253, 0.9771) 0.0386	0.0364	
North America	60	23 (38.3)	37 (61.7)	11.1 (3.3, NE)	33	14 (42.4)	19 (57.6)	4.4 (1.6, NE)	0.6255 (0.3164, 1.2364) 0.1771	0.1718	
Europe + Israel	166	64 (38.6)	102 (61.4)	15.3 (9.7, NE)	85	32 (37.6)	53 (62.4)	7.5 (5.4, NE)	0.8075 (0.5263, 1.2388) 0.3275	0.3238	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	200	83 (41.5)	117 (58.5)	16.3 (11.1, NE)	105	47 (44.8)	58 (55.2)	6.7 (4.4, 11.4)	0.6508 (0.4525, 0.9359) 0.0205	0.0191	0.5417
1	173	69 (39.9)	104 (60.1)	10.9 (7.6, NE)	79	34 (43.0)	45 (57.0)	7.0 (4.2, NE)	0.7616 (0.5027, 1.1539) 0.1990	0.1954	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.2545
0	60	28 (46.7)	32 (53.3)	9.2 (4.4, NE)	34	13 (38.2)	21 (61.8)	5.9 (2.7, NE)	0.8797 (0.4491, 1.7233) 0.7087	0.7044	
1	108	40 (37.0)	68 (63.0)	22.3 (8.3, NE)	51	17 (33.3)	34 (66.7)	NE (5.9, NE)	0.9670 (0.5460, 1.7125) 0.9084	0.9089	
2	115	46 (40.0)	69 (60.0)	NE (7.7, NE)	54	29 (53.7)	25 (46.3)	4.5 (1.4, 7.9)	0.5355 (0.3338, 0.8591) 0.0096	0.0082	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	38 (42.2)	52 (57.8)	16.3 (6.7, NE)	45	22 (48.9)	23 (51.1)	5.8 (2.1, NE)	0.5923 (0.3458, 1.0145) 0.0565	0.0530	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.1664
PD	174	62 (35.6)	112 (64.4)	NE (10.9, NE)	85	39 (45.9)	46 (54.1)	5.9 (2.1, 8.5)	0.5254 (0.3499, 0.7889) 0.0019	0.0016	
PR	48	19 (39.6)	29 (60.4)	14.7 (9.2, NE)	22	8 (36.4)	14 (63.6)	6.7 (1.0, NE)	0.6927 (0.2986, 1.6070) 0.3925	0.3906	
SD	82	35 (42.7)	47 (57.3)	11.1 (6.2, NE)	55	22 (40.0)	33 (60.0)	11.4 (5.7, NE)	0.9733 (0.5689, 1.6650) 0.9212	0.9163	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.9521
Yes	37	11 (29.7)	26 (70.3)	22.3 (9.5, NE)	15	3 (20.0)	12 (80.0)	NE (0.8, NE)	0.6949 (0.1866, 2.5871) 0.5873	0.5880
No	336	141 (42.0)	195 (58.0)	14.7 (9.2, NE)	169	78 (46.2)	91 (53.8)	6.7 (4.5, 8.5)	0.7180 (0.5428, 0.9499) 0.0203	0.0190

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.6737
Yes	24	5 (20.8)	19 (79.2)	NE (NE, NE)	8	2 (25.0)	6 (75.0)	NE (0.8, NE)	0.5342 (0.1012, 2.8204) 0.4602	0.4557
No	349	147 (42.1)	202 (57.9)	14.7 (9.5, 23.0)	176	79 (44.9)	97 (55.1)	6.7 (4.6, 8.5)	0.7176 (0.5440, 0.9466) 0.0188	0.0176

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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## Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.7372
Normal Function	202	79 (39.1)	123 (60.9)	22.3 (10.4, NE)	87	38 (43.7)	49 (56.3)	5.7 (4.2, 9.8)	0.6523 (0.4397, 0.9676) 0.0337	0.0309	
Mild Impairment	123	56 (45.5)	67 (54.5)	10.3 (6.7, 23.0)	69	30 (43.5)	39 (56.5)	6.7 (4.2, NE)	0.7535 (0.4799, 1.1831) 0.2189	0.2175	
Moderate Impairment	41	15 (36.6)	26 (63.4)	NE (5.6, NE)	23	11 (47.8)	12 (52.2)	7.0 (1.6, NE)	0.7825 (0.3589, 1.7058) 0.5373	0.5367	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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## Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.5829
Normal Function	170	79 (46.5)	91 (53.5)	14.7 (6.7, NE)	98	47 (48.0)	51 (52.0)	6.1 (4.2, 11.4)	0.7732 (0.5364, 1.1145) 0.1680	0.1616
Mild Impairment	195	71 (36.4)	124 (63.6)	23.0 (10.9, NE)	84	33 (39.3)	51 (60.7)	6.7 (4.4, NE)	0.6375 (0.4191, 0.9696) 0.0354	0.0335

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline visceral disease										0.4556
Yes	332	137 (41.3)	195 (58.7)	15.3 (9.7, 23.0)	157	68 (43.3)	89 (56.7)	7.0 (4.7, 11.4)	0.7258 (0.5409, 0.9738) 0.0326	0.0310
No	41	15 (36.6)	26 (63.4)	NE (7.2, NE)	27	13 (48.1)	14 (51.9)	5.9 (1.6, NE)	0.5181 (0.2427, 1.1060) 0.0892	0.0834

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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## Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.7539
Positive	331	136 (41.1)	195 (58.9)	15.4 (10.3, NE)	163	72 (44.2)	91 (55.8)	6.7 (4.6, 9.8)	0.6908 (0.5173, 0.9225) 0.0122	0.0114	
Negative	42	16 (38.1)	26 (61.9)	10.9 (2.8, NE)	21	9 (42.9)	12 (57.1)	7.0 (1.7, NE)	0.7832 (0.3401, 1.8034) 0.5658	0.5588	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Systemic Therapy Side Effects

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.1702
Positive	333	136 (40.8)	197 (59.2)	15.4 (10.3, NE)	166	76 (45.8)	90 (54.2)	6.1 (4.4, 8.5)	0.6586 (0.4955, 0.8753) 0.0040	0.0037	
Negative	40	16 (40.0)	24 (60.0)	10.9 (2.8, NE)	18	5 (27.8)	13 (72.2)	7.0 (1.7, NE)	1.3446 (0.4870, 3.7127) 0.5677	0.5655	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.7926
HER2 IHC 1+	214	39 (18.2)	175 (81.8)	NE (NE, NE)	107	14 (13.1)	93 (86.9)	NE (NE, NE)	1.0053 (0.5420, 1.8644) 0.9867	0.9877	
HER2 IHC 2+/ISH Negative	159	23 (14.5)	136 (85.5)	NE (NE, NE)	77	9 (11.7)	68 (88.3)	NE (NE, NE)	0.6754 (0.3081, 1.4808) 0.3272	0.3248	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.6114
1	221	37 (16.7)	184 (83.3)	NE (NE, NE)	100	12 (12.0)	88 (88.0)	NE (NE, NE)	0.9732 (0.5032, 1.8821) 0.9356	0.9357	
>=2	151	25 (16.6)	126 (83.4)	NE (NE, NE)	83	11 (13.3)	72 (86.7)	NE (NE, NE)	0.7210 (0.3484, 1.4920) 0.3779	0.3763	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.7480
Yes	235	41 (17.4)	194 (82.6)	NE (NE, NE)	118	15 (12.7)	103 (87.3)	NE (NE, NE)	0.9019 (0.4940, 1.6463) 0.7365	0.7353	
No	98	14 (14.3)	84 (85.7)	NE (NE, NE)	48	6 (12.5)	42 (87.5)	NE (NE, NE)	0.7331 (0.2780, 1.9334) 0.5303	0.5289	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Age										0.0137
<65	290	47 (16.2)	243 (83.8)	NE (NE, NE)	136	21 (15.4)	115 (84.6)	NE (NE, NE)	0.6165 (0.3649, 1.0416)	0.0679
>=65	83	15 (18.1)	68 (81.9)	NE (17.1, NE)	48	2 (4.2)	46 (95.8)	NE (NE, NE)	3.4694 (0.7832, 15.3678)	0.0815

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2651
<75	359	61 (17.0)	298 (83.0)	NE (NE, NE)	175	23 (13.1)	152 (86.9)	NE (NE, NE)	0.7943 (0.4872, 1.2952) 0.3559	0.3545	
>=75	14	1 (7.1)	13 (92.9)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9984	0.3865	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.3747
White	176	23 (13.1)	153 (86.9)	NE (NE, NE)	91	11 (12.1)	80 (87.9)	NE (NE, NE)	0.6615 (0.3165, 1.3826) 0.2719	0.2683	
Non-White	197	39 (19.8)	158 (80.2)	NE (NE, NE)	92	12 (13.0)	80 (87.0)	NE (NE, NE)	1.0174 (0.5278, 1.9613) 0.9588	0.9589	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.6310
Asia	147	30 (20.4)	117 (79.6)	NE (NE, NE)	66	10 (15.2)	56 (84.8)	NE (NE, NE)	0.8615 (0.4163, 1.7827) 0.6878	0.6868	
North America	60	9 (15.0)	51 (85.0)	NE (NE, NE)	33	2 (6.1)	31 (93.9)	NE (NE, NE)	1.8752 (0.3984, 8.8270) 0.4264	0.4174	
Europe + Israel	166	23 (13.9)	143 (86.1)	NE (NE, NE)	85	11 (12.9)	74 (87.1)	NE (NE, NE)	0.6571 (0.3151, 1.3701) 0.2627	0.2593	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
ECOG PS											0.9394
0	200	32 (16.0)	168 (84.0)	NE (NE, NE)	105	12 (11.4)	93 (88.6)	NE (NE, NE)	0.8611 (0.4389, 1.6892)	0.6627	
1	173	30 (17.3)	143 (82.7)	NE (NE, NE)	79	11 (13.9)	68 (86.1)	NE (NE, NE)	0.8410 (0.4151, 1.7038)	0.6299	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.3954
0	60	10 (16.7)	50 (83.3)	NE (NE, NE)	34	4 (11.8)	30 (88.2)	NE (7.1, NE)	0.9881 (0.3075, 3.1756) 0.9840	0.9840
1	108	20 (18.5)	88 (81.5)	NE (NE, NE)	51	5 (9.8)	46 (90.2)	NE (NE, NE)	1.6372 (0.6129, 4.3728) 0.3254	0.3209
2	115	20 (17.4)	95 (82.6)	NE (NE, NE)	54	8 (14.8)	46 (85.2)	NE (NE, NE)	0.5945 (0.2496, 1.4158) 0.2401	0.2354

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	12 (13.3)	78 (86.7)	NE (17.1, NE)	45	6 (13.3)	39 (86.7)	NE (NE, NE)	0.4885 (0.1735, 1.3756) 0.1750	0.1673	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.9275
PD	174	30 (17.2)	144 (82.8)	NE (17.1, NE)	85	12 (14.1)	73 (85.9)	NE (NE, NE)	0.6936 (0.3476, 1.3840) 0.2992	0.2971	
PR	48	9 (18.8)	39 (81.3)	NE (15.4, NE)	22	2 (9.1)	20 (90.9)	NE (NE, NE)	1.0790 (0.2198, 5.2980) 0.9253	0.9253	
SD	82	8 (9.8)	74 (90.2)	NE (NE, NE)	55	5 (9.1)	50 (90.9)	NE (NE, NE)	0.9192 (0.2988, 2.8275) 0.8831	0.8831	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.6838
Yes	37	6 (16.2)	31 (83.8)	NE (13.1, NE)	15	1 (6.7)	14 (93.3)	NE (3.0, NE)	1.1693 (0.1338, 10.2167)	0.8874
No	336	56 (16.7)	280 (83.3)	NE (NE, NE)	169	22 (13.0)	147 (87.0)	NE (NE, NE)	0.8381 (0.5073, 1.3845)	0.4893

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.9552
Yes	24	4 (16.7)	20 (83.3)	NE (13.1, NE)	8	1 (12.5)	7 (87.5)	NE (3.0, NE)	0.6856 (0.0715, 6.5785) 0.7435	0.7422	
No	349	58 (16.6)	291 (83.4)	NE (NE, NE)	176	22 (12.5)	154 (87.5)	NE (NE, NE)	0.8642 (0.5246, 1.4236) 0.5665	0.5654	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0046
Normal Function	202	29 (14.4)	173 (85.6)	NE (NE, NE)	87	11 (12.6)	76 (87.4)	NE (NE, NE)	0.6618 (0.3257, 1.3446) 0.2537	0.2508	
Mild Impairment	123	23 (18.7)	100 (81.3)	NE (17.1, NE)	69	11 (15.9)	58 (84.1)	NE (NE, NE)	0.6096 (0.2884, 1.2889) 0.1951	0.1910	
Moderate Impairment	41	9 (22.0)	32 (78.0)	NE (12.3, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9930	0.0209	

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[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.5673
Normal Function	170	27 (15.9)	143 (84.1)	NE (NE, NE)	98	13 (13.3)	85 (86.7)	NE (NE, NE)	0.7403 (0.3761, 1.4571)	0.3827
Mild Impairment	195	34 (17.4)	161 (82.6)	NE (NE, NE)	84	9 (10.7)	75 (89.3)	NE (NE, NE)	0.9982 (0.4734, 2.1050)	0.9958

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 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Symptom Scales/Breast Symptoms

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1686
Yes	332	56 (16.9)	276 (83.1)	NE (NE, NE)	157	18 (11.5)	139 (88.5)	NE (NE, NE)	1.0000 (0.5842, 1.7116)	0.9978	
No	41	6 (14.6)	35 (85.4)	NE (17.1, NE)	27	5 (18.5)	22 (81.5)	NE (5.7, NE)	0.2644 (0.0646, 1.0831)	0.0497	

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 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.6426
Positive	331	55 (16.6)	276 (83.4)	NE (NE, NE)	163	21 (12.9)	142 (87.1)	NE (NE, NE)	0.8520 (0.5117, 1.4187)	0.5370	
Negative	42	7 (16.7)	35 (83.3)	17.1 (11.8, NE)	21	2 (9.5)	19 (90.5)	NE (5.3, NE)	0.6544 (0.1136, 3.7694)	0.6329	

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Symptom Scales/Breast Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.6037
Positive	333	54 (16.2)	279 (83.8)	NE (NE, NE)	166	21 (12.7)	145 (87.3)	NE (NE, NE)	0.8431 (0.5054, 1.4064) 0.5134	0.5122	
Negative	40	8 (20.0)	32 (80.0)	17.1 (11.8, NE)	18	2 (11.1)	16 (88.9)	NE (5.3, NE)	0.7997 (0.1499, 4.2654) 0.7935	0.7931	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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[c] Two-sided p-value from unstratified log-rank test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.7201
HER2 IHC 1+	214	68 (31.8)	146 (68.2)	23.0 (14.4, NE)	107	32 (29.9)	75 (70.1)	9.1 (7.0, NE)	0.6343 (0.4113, 0.9780) 0.0393	0.0378	
HER2 IHC 2+/ISH Negative	159	56 (35.2)	103 (64.8)	18.4 (11.8, NE)	77	30 (39.0)	47 (61.0)	6.1 (4.7, NE)	0.5506 (0.3479, 0.8716) 0.0109	0.0097	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.0686
1	221	81 (36.7)	140 (63.3)	16.2 (12.5, NE)	100	33 (33.0)	67 (67.0)	16.9 (7.1, NE)	0.7890 (0.5226, 1.1912)	0.2513	
>=2	151	43 (28.5)	108 (71.5)	19.0 (14.4, NE)	83	29 (34.9)	54 (65.1)	7.0 (3.3, NE)	0.3682 (0.2224, 0.6096)	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.0649
Yes	235	78 (33.2)	157 (66.8)	17.2 (12.5, NE)	118	34 (28.8)	84 (71.2)	16.9 (8.7, NE)	0.7368 (0.4871, 1.1144) 0.1480	0.1444	
No	98	35 (35.7)	63 (64.3)	18.4 (13.4, NE)	48	23 (47.9)	25 (52.1)	6.1 (1.9, NE)	0.3777 (0.2184, 0.6530) 0.0005	0.0003	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8225
<65	290	99 (34.1)	191 (65.9)	17.2 (13.3, NE)	136	46 (33.8)	90 (66.2)	8.7 (5.1, NE)	0.5790 (0.4029, 0.8320) 0.0031	0.0027	
>=65	83	25 (30.1)	58 (69.9)	18.4 (16.2, NE)	48	16 (33.3)	32 (66.7)	NE (5.6, NE)	0.6438 (0.3375, 1.2281) 0.1815	0.1807	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Age										0.2329
<75	359	121 (33.7)	238 (66.3)	18.4 (13.4, NE)	175	61 (34.9)	114 (65.1)	8.7 (5.6, NE)	0.5551 (0.4032, 0.7642) 0.0003	0.0002
>=75	14	3 (21.4)	11 (78.6)	NE (3.3, NE)	9	1 (11.1)	8 (88.9)	NE (3.3, NE)	2.3685 (0.2460, 22.8041) 0.4555	0.4343

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.9845
White	176	53 (30.1)	123 (69.9)	23.0 (12.5, NE)	91	28 (30.8)	63 (69.2)	16.9 (5.1, NE)	0.5798 (0.3617, 0.9293) 0.0235	0.0215	
Non-White	197	71 (36.0)	126 (64.0)	17.2 (13.8, NE)	92	34 (37.0)	58 (63.0)	9.1 (5.9, NE)	0.5998 (0.3928, 0.9159) 0.0179	0.0168	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.7657
Asia	147	62 (42.2)	85 (57.8)	16.4 (13.4, 19.0)	66	27 (40.9)	39 (59.1)	9.1 (2.8, NE)	0.6319 (0.3965, 1.0070) 0.0535	0.0517	
North America	60	15 (25.0)	45 (75.0)	NE (11.2, NE)	33	10 (30.3)	23 (69.7)	4.7 (3.1, NE)	0.3841 (0.1635, 0.9020) 0.0280	0.0231	
Europe + Israel	166	47 (28.3)	119 (71.7)	23.0 (12.8, NE)	85	25 (29.4)	60 (70.6)	16.9 (7.0, NE)	0.6085 (0.3694, 1.0023) 0.0511	0.0480	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	200	68 (34.0)	132 (66.0)	18.4 (14.4, NE)	105	39 (37.1)	66 (62.9)	8.7 (3.3, NE)	0.4439 (0.2938, 0.6706)	<0.0001	0.0564
1	173	56 (32.4)	117 (67.6)	19.0 (10.6, NE)	79	23 (29.1)	56 (70.9)	NE (6.1, NE)	0.8583 (0.5238, 1.4064)	0.5442	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.8698
0	60	21 (35.0)	39 (65.0)	NE (6.7, NE)	34	13 (38.2)	21 (61.8)	5.9 (1.6, NE)	0.5483 (0.2700, 1.1136) 0.0965	0.0921	
1	108	33 (30.6)	75 (69.4)	NE (11.8, NE)	51	17 (33.3)	34 (66.7)	16.9 (4.7, NE)	0.6911 (0.3825, 1.2488) 0.2210	0.2167	
2	115	37 (32.2)	78 (67.8)	19.0 (13.3, NE)	54	18 (33.3)	36 (66.7)	7.0 (3.7, NE)	0.4916 (0.2681, 0.9012) 0.0217	0.0191	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	33 (36.7)	57 (63.3)	16.4 (13.4, NE)	45	14 (31.1)	31 (68.9)	9.1 (3.8, NE)	0.6318 (0.3271, 1.2201)	0.1676 0.1714

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.8181
PD	174	48 (27.6)	126 (72.4)	19.0 (13.4, NE)	85	24 (28.2)	61 (71.8)	NE (5.6, NE)	0.5997 (0.3601, 0.9987) 0.0494	0.0469	
PR	48	17 (35.4)	31 (64.6)	NE (10.2, NE)	22	8 (36.4)	14 (63.6)	7.0 (1.6, NE)	0.4526 (0.1874, 1.0930) 0.0780	0.0709	
SD	82	31 (37.8)	51 (62.2)	18.4 (11.2, NE)	55	21 (38.2)	34 (61.8)	16.9 (4.7, NE)	0.6437 (0.3636, 1.1397) 0.1307	0.1266	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.0706
Yes	37	11 (29.7)	26 (70.3)	NE (9.8, NE)	15	1 (6.7)	14 (93.3)	NE (1.6, NE)	2.2701 (0.2834, 18.1862) 0.4400	0.4248
No	336	113 (33.6)	223 (66.4)	18.4 (13.8, NE)	169	61 (36.1)	108 (63.9)	9.1 (5.6, NE)	0.5635 (0.4081, 0.7780) 0.0005	0.0004

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.3740
Yes	24	9 (37.5)	15 (62.5)	NE (4.9, NE)	8	2 (25.0)	6 (75.0)	NE (1.6, NE)	1.0814 (0.2285, 5.1180) 0.9214	0.9197	
No	349	115 (33.0)	234 (67.0)	18.4 (13.8, NE)	176	60 (34.1)	116 (65.9)	9.1 (5.9, NE)	0.5731 (0.4147, 0.7919) 0.0007	0.0006	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.4012
Normal Function	202	62 (30.7)	140 (69.3)	NE (13.3, NE)	87	29 (33.3)	58 (66.7)	8.7 (5.1, NE)	0.5128 (0.3236, 0.8127) 0.0045	0.0038	
Mild Impairment	123	47 (38.2)	76 (61.8)	16.4 (12.5, 19.0)	69	25 (36.2)	44 (63.8)	9.1 (3.2, NE)	0.5716 (0.3442, 0.9494) 0.0307	0.0292	
Moderate Impairment	41	14 (34.1)	27 (65.9)	NE (7.4, NE)	23	7 (30.4)	16 (69.6)	NE (4.7, NE)	1.0676 (0.4282, 2.6616) 0.8884	0.8850	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.4521
Normal Function	170	60 (35.3)	110 (64.7)	NE (13.4, NE)	98	37 (37.8)	61 (62.2)	9.1 (5.4, NE)	0.5673 (0.3716, 0.8662) 0.0087	0.0077	
Mild Impairment	195	62 (31.8)	133 (68.2)	17.2 (11.8, NE)	84	24 (28.6)	60 (71.4)	16.9 (5.1, NE)	0.6395 (0.3930, 1.0406) 0.0719	0.0704	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.2583
Yes	332	109 (32.8)	223 (67.2)	18.4 (13.4, NE)	157	50 (31.8)	107 (68.2)	16.9 (7.0, NE)	0.6305 (0.4468, 0.8896) 0.0086	0.0081	
No	41	15 (36.6)	26 (63.4)	NE (10.0, NE)	27	12 (44.4)	15 (55.6)	4.5 (1.6, NE)	0.4614 (0.2050, 1.0385) 0.0617	0.0550	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.8881
Positive	331	112 (33.8)	219 (66.2)	17.2 (13.4, NE)	163	55 (33.7)	108 (66.3)	9.1 (6.1, NE)	0.5948 (0.4265, 0.8296) 0.0022	0.0020	
Negative	42	12 (28.6)	30 (71.4)	19.0 (10.0, NE)	21	7 (33.3)	14 (66.7)	NE (3.1, NE)	0.6109 (0.2309, 1.6160) 0.3207	0.3119	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Arm Symptoms

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.6976
Positive	333	112 (33.6)	221 (66.4)	18.4 (13.4, NE)	166	57 (34.3)	109 (65.7)	9.1 (5.6, NE)	0.5809 (0.4180, 0.8074) 0.0012	0.0010	
Negative	40	12 (30.0)	28 (70.0)	19.0 (10.0, NE)	18	5 (27.8)	13 (72.2)	NE (1.7, NE)	0.7762 (0.2638, 2.2839) 0.6455	0.6441	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.8975
HER2 IHC 1+	214	18 (8.4)	196 (91.6)	12.9 (3.0, NE)	107	6 (5.6)	101 (94.4)	NE (1.2, NE)	0.9769 (0.3851, 2.4781)	0.9614	
HER2 IHC 2+/ISH Negative	159	14 (8.8)	145 (91.2)	NE (6.7, NE)	77	5 (6.5)	72 (93.5)	NE (2.7, NE)	1.0608 (0.3788, 2.9709)	0.9140	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.2876
1	221	23 (10.4)	198 (89.6)	12.5 (2.9, NE)	100	7 (7.0)	93 (93.0)	NE (2.7, NE)	1.4227 (0.6073, 3.3325) 0.4170	0.4144
>=2	151	9 (6.0)	142 (94.0)	NE (9.7, NE)	83	4 (4.8)	79 (95.2)	NE (0.7, NE)	0.5610 (0.1708, 1.8422) 0.3407	0.3321

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.8773
Yes	235	19 (8.1)	216 (91.9)	NE (7.2, NE)	118	7 (5.9)	111 (94.1)	NE (2.7, NE)	0.7798 (0.3212, 1.8930)	0.5780	
No	98	9 (9.2)	89 (90.8)	NE (1.4, NE)	48	4 (8.3)	44 (91.7)	NE (0.7, NE)	0.9003 (0.2769, 2.9271)	0.8618	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											0.6001
<65	290	27 (9.3)	263 (90.7)	12.9 (7.2, NE)	136	7 (5.1)	129 (94.9)	NE (2.1, NE)	1.1241 (0.4859, 2.6001) 0.7846	0.7901	
>=65	83	5 (6.0)	78 (94.0)	NE (2.8, NE)	48	4 (8.3)	44 (91.7)	NE (0.7, NE)	0.8242 (0.2205, 3.0811) 0.7738	0.7853	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											1.0000
<75	359	32 (8.9)	327 (91.1)	NE (7.2, NE)	175	11 (6.3)	164 (93.7)	NE (6.0, NE)	1.0040 (0.5026, 2.0056) 0.9910	0.9916	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.0791
White	176	11 (6.3)	165 (93.8)	NE (7.2, NE)	91	7 (7.7)	84 (92.3)	NE (1.2, NE)	0.5567 (0.2121, 1.4614) 0.2342	0.2287	
Non-White	197	21 (10.7)	176 (89.3)	12.5 (2.9, NE)	92	4 (4.3)	88 (95.7)	NE (6.0, NE)	1.8383 (0.6270, 5.3891) 0.2672	0.2614	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.1123
Asia	147	15 (10.2)	132 (89.8)	7.4 (1.4, NE)	66	4 (6.1)	62 (93.9)	NE (2.1, NE)	1.7994 (0.5949, 5.4425) 0.2982	0.2935	
North America	60	1 (1.7)	59 (98.3)	NE (4.2, NE)	33	2 (6.1)	31 (93.9)	NE (1.0, NE)	0.1121 (0.0096, 1.3098) 0.0810	0.0385	
Europe + Israel	166	16 (9.6)	150 (90.4)	12.9 (7.2, NE)	85	5 (5.9)	80 (94.1)	NE (1.2, NE)	1.0415 (0.3790, 2.8622) 0.9372	0.9285	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
ECOG PS										0.7389
0	200	15 (7.5)	185 (92.5)	12.9 (1.6, NE)	105	7 (6.7)	98 (93.3)	6.0 (2.1, NE)	0.9959 (0.4007, 2.4752)	0.9869
1	173	17 (9.8)	156 (90.2)	NE (7.2, NE)	79	4 (5.1)	75 (94.9)	NE (0.8, NE)	1.2365 (0.4138, 3.6944)	0.6988

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.2134
0	60	4 (6.7)	56 (93.3)	NE (0.7, NE)	34	1 (2.9)	33 (97.1)	NE (0.7, NE)	1.4709 (0.1620, 13.3567) 0.7318	0.7141
1	108	15 (13.9)	93 (86.1)	4.2 (2.8, NE)	51	3 (5.9)	48 (94.1)	NE (0.8, NE)	1.7388 (0.5026, 6.0153) 0.3823	0.3680
2	115	6 (5.2)	109 (94.8)	NE (NE, NE)	54	5 (9.3)	49 (90.7)	NE (0.7, NE)	0.3809 (0.1126, 1.2879) 0.1204	0.1076

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	7 (7.8)	83 (92.2)	NE (6.2, NE)	45	2 (4.4)	43 (95.6)	NE (1.2, NE)	1.1431 (0.2241, 5.8300) 0.8722	0.8721

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.0448
PD	174	15 (8.6)	159 (91.4)	NE (6.2, NE)	85	2 (2.4)	83 (97.6)	NE (NE, NE)	2.5105 (0.5711, 11.0364) 0.2231	0.2080	
PR	48	5 (10.4)	43 (89.6)	12.9 (0.7, NE)	22	0	22 (100)	NE (NE, NE)	NE (NE, NE) 0.9971	0.1591	
SD	82	5 (6.1)	77 (93.9)	NE (2.8, NE)	55	7 (12.7)	48 (87.3)	6.0 (0.8, NE)	0.5018 (0.1541, 1.6336) 0.2522	0.2460	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Reported history of CNS metastases											0.2801
Yes	37	2 (5.4)	35 (94.6)	NE (3.0, NE)	15	1 (6.7)	14 (93.3)	6.0 (NE, NE)	0.2930 (0.0261, 3.2872)	0.2902	
No	336	30 (8.9)	306 (91.1)	12.9 (6.2, NE)	169	10 (5.9)	159 (94.1)	NE (2.7, NE)	1.2022 (0.5848, 2.4715)	0.6160	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)			TPC (N=184)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.5853
Yes	24	2 (8.3)	22 (91.7)	NE (1.4, NE)	8	0	8 (100)	NE (NE, NE)	0.9981	0.6270
No	349	30 (8.6)	319 (91.4)	12.9 (6.7, NE)	176	11 (6.3)	165 (93.8)	NE (6.0, NE)	1.0650 (0.5308, 2.1367)	0.8596

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.5997
Normal Function	202	19 (9.4)	183 (90.6)	NE (3.0, NE)	87	3 (3.4)	84 (96.6)	NE (2.1, NE)	1.8132 (0.5339, 6.1581) 0.3401	0.3378	
Mild Impairment	123	11 (8.9)	112 (91.1)	12.5 (2.8, NE)	69	7 (10.1)	62 (89.9)	NE (0.8, NE)	0.7880 (0.3021, 2.0557) 0.6263	0.6317	
Moderate Impairment	41	2 (4.9)	39 (95.1)	NE (0.7, NE)	23	1 (4.3)	22 (95.7)	NE (0.7, NE)	0.5316 (0.0478, 5.9095) 0.6071	0.6012	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 10JAN2023 – 19:36; Program name: T3\_EQ5D\_FD\_2\_FAS.sas; Output name: T33BR45.rtf

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.8179
Normal Function	170	16 (9.4)	154 (90.6)	12.9 (2.9, NE)	98	6 (6.1)	92 (93.9)	NE (2.7, NE)	1.0951 (0.4196, 2.8585) 0.8527	0.8548	
Mild Impairment	195	16 (8.2)	179 (91.8)	NE (7.2, NE)	84	5 (6.0)	79 (94.0)	NE (1.2, NE)	0.9656 (0.3518, 2.6503) 0.9458	0.9434	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.8640
Yes	332	26 (7.8)	306 (92.2)	NE (7.4, NE)	157	9 (5.7)	148 (94.3)	NE (6.0, NE)	1.0114 (0.4710, 2.1717) 0.9769	0.9772	
No	41	6 (14.6)	35 (85.4)	NE (0.7, NE)	27	2 (7.4)	25 (92.6)	NE (1.2, NE)	1.1065 (0.2227, 5.4972) 0.9015	0.9111	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Run date: 10JAN2023 – 19:36; Program name: T3\_EQ5D\_FD\_2\_FAS.sas; Output name: T33BR45.rtf

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.1118
Positive	331	29 (8.8)	302 (91.2)	NE (7.2, NE)	163	11 (6.7)	152 (93.3)	NE (2.7, NE)	0.8916 (0.4424, 1.7966)	0.7458	
Negative	42	3 (7.1)	39 (92.9)	7.4 (0.7, NE)	21	0	21 (100)	NE (NE, NE)	NE (NE, NE)	0.2446	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Run date: 10JAN2023 – 19:36; Program name: T3\_EQ5D\_FD\_2\_FAS.sas; Output name: T33BR45.rtf

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Symptom Scales/Upset by Hair Loss

Subgroup	T-DXd (N=373)				TPC (N=184)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.0714
Positive	333	28 (8.4)	305 (91.6)	NE (9.7, NE)	166	11 (6.6)	155 (93.4)	NE (2.7, NE)	0.8659 (0.4280, 1.7517) 0.6887	0.6892	
Negative	40	4 (10.0)	36 (90.0)	7.4 (1.4, NE)	18	0	18 (100)	NE (NE, NE)	NE (NE, NE) 0.9971	0.1483	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

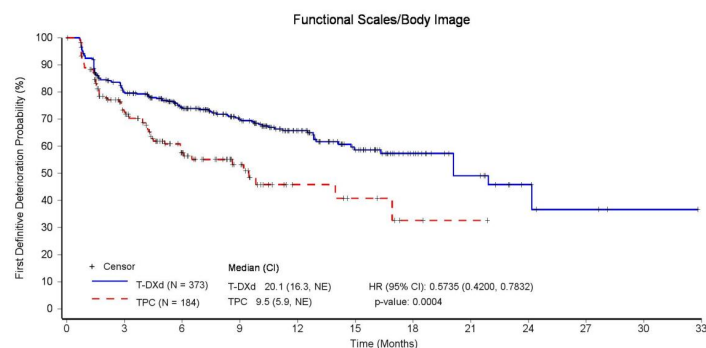
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Patients still at risk:

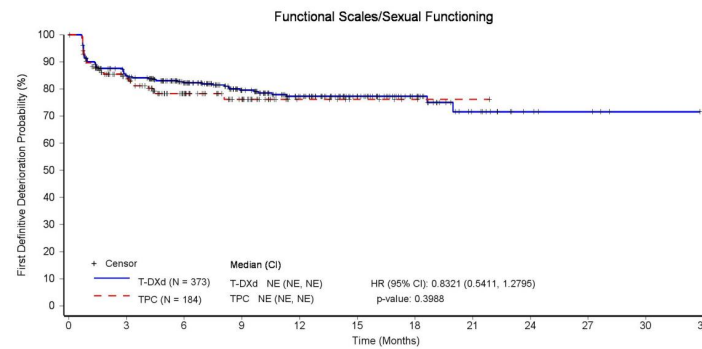
T-DXd (N = 373)	373	257	196	146	93	56	32	18	6	3	1	0
TPC (N = 184)	184	96	51	26	9	6	2	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

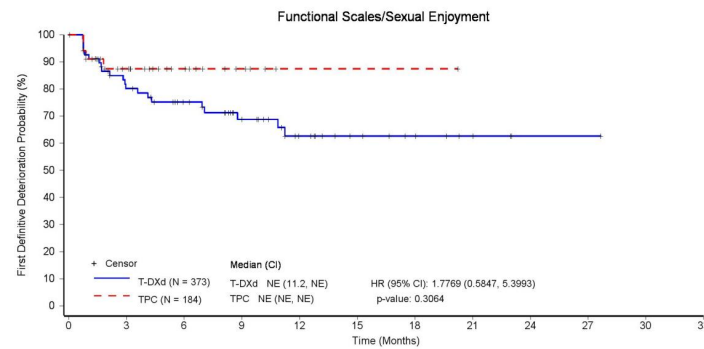
T-DXd (N = 373)	373	267	212	159	107	68	40	17	6	4	1	0
TPC (N = 184)	184	101	56	31	9	5	2	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

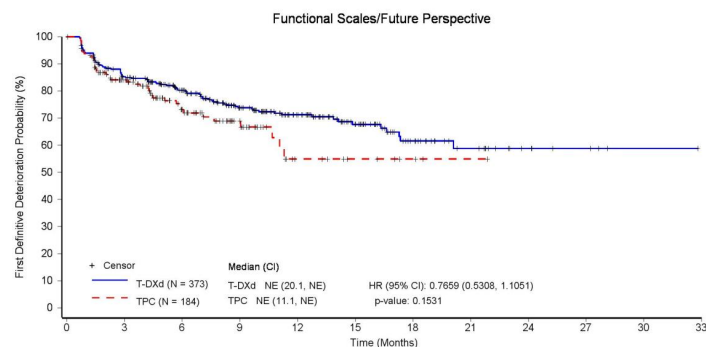
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	50	40	28	16	10	7	4	1	1	0	0
TPC (N = 184)	184	21	11	5	1	1	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

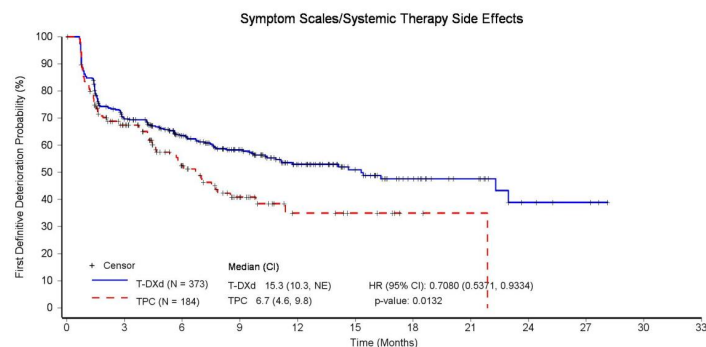
T-DXd (N = 373)	373	279	221	160	107	66	34	20	7	4	1	0
TPC (N = 184)	184	113	62	32	10	6	3	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

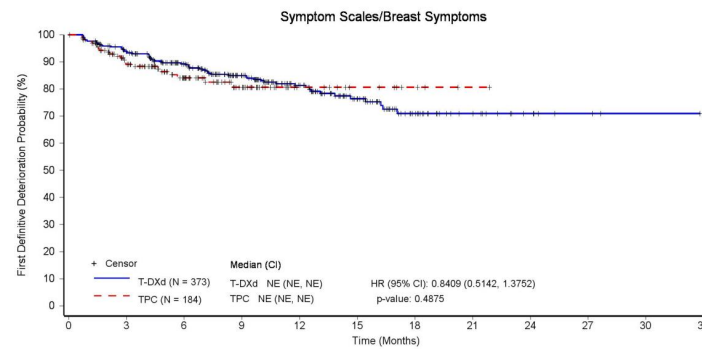
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	226	166	125	79	48	28	16	5	3	0	0
TPC (N = 184)	184	92	49	24	9	6	2	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:37; Program name: F3\_EQ5D\_FD\_3\_FAS.sas; Output name: F34BR45.rtf

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Patients still at risk:

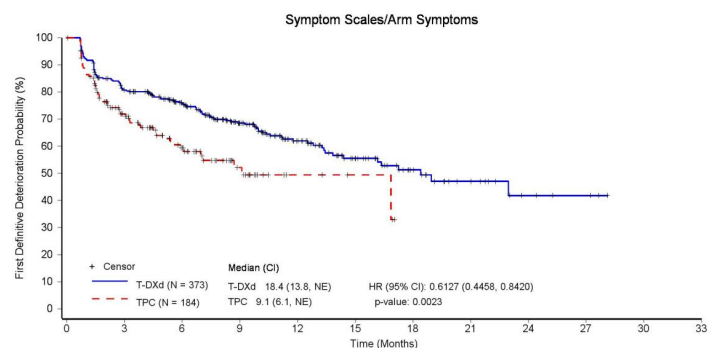
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	297	239	184	120	72	37	18	7	3	1	0
TPC (N = 184)	184	117	67	36	13	8	4	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

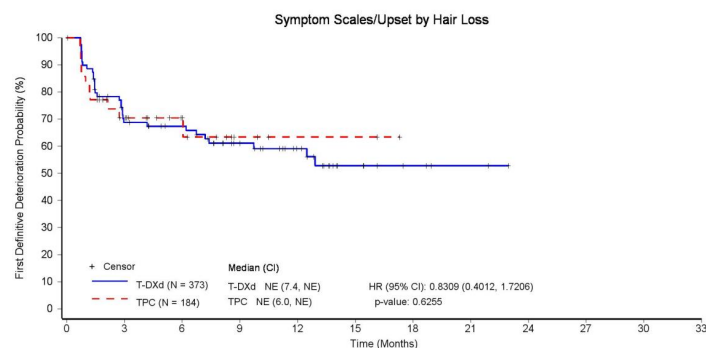
T-DXd (N = 373)	373	263	208	147	84	50	28	15	5	3	0	0
TPC (N = 184)	184	91	48	19	5	3	0	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 373)	373	50	44	31	21	9	4	2	0	0	0	0
TPC (N = 184)	184	20	11	4	2	2	0	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

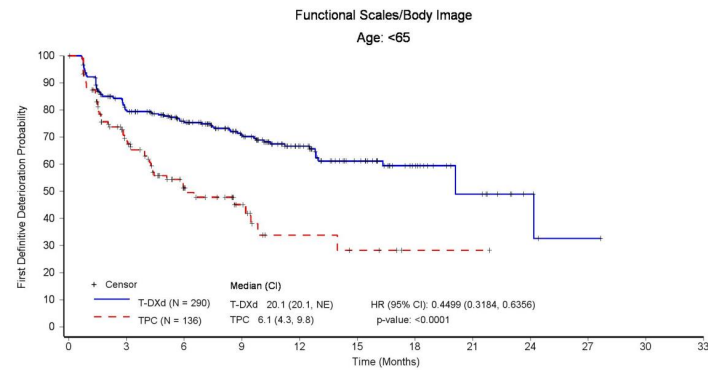
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 290)	290	200	157	113	71	43	26	14	4	1	0	0
TPC (N = 136)	136	65	31	15	6	4	1	1	0	0	0	0

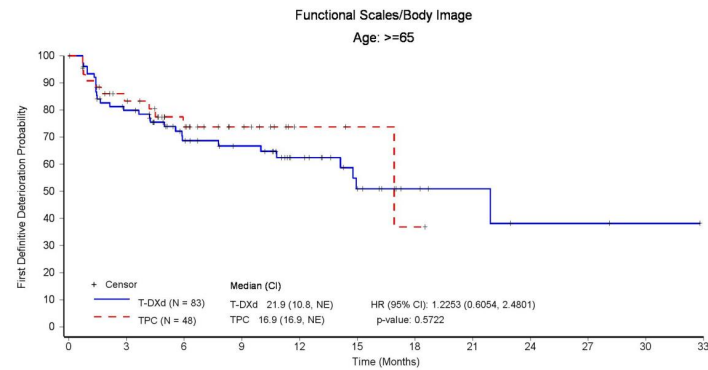
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

T-DXd (N = 83)	83	57	39	33	22	13	6	4	2	2	1	0
TPC (N = 48)	48	31	20	11	3	2	1	0	0	0	0	0

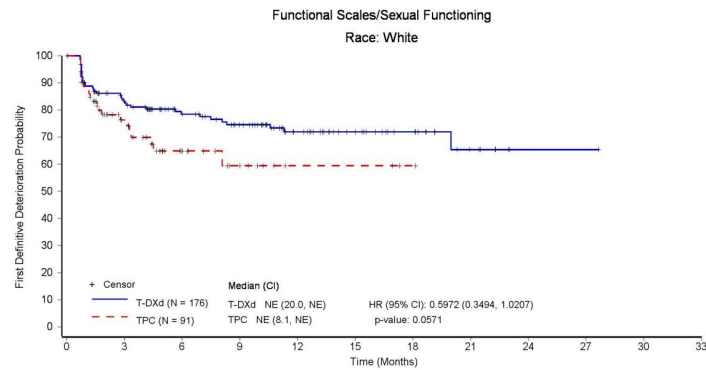
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 176)	176	114	86	72	46	30	20	8	1	1	0	0
TPC (N = 91)	91	37	17	9	3	3	1	0	0	0	0	0

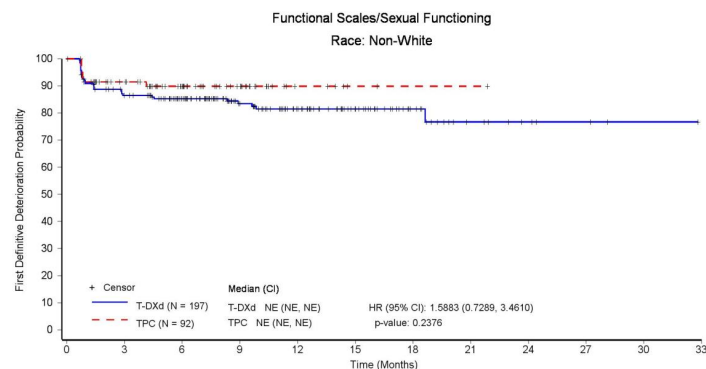
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.7.4.4 - EORTC QLQ-BR45 - Definitive deterioration 10 Points - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - Full Analysis Set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 197)	197	153	126	87	61	38	20	9	5	3	1	0
TPC (N = 92)	92	63	39	22	6	2	1	1	0	0	0	0

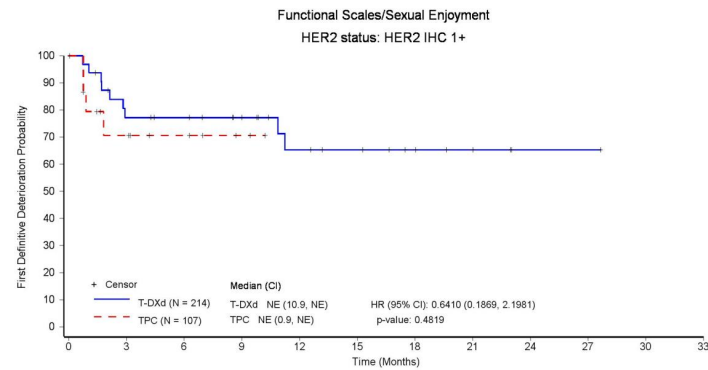
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:37; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F35BR45.rtf

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DE.F.7.4.4 - EORTC QLQ-BR45 - Definitive deterioration 10 Points - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - Full Analysis Set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 214)	214	23	21	17	11	9	6	4	1	1	0	0
TPC (N = 107)	107	8	5	2	0	0	0	0	0	0	0	0

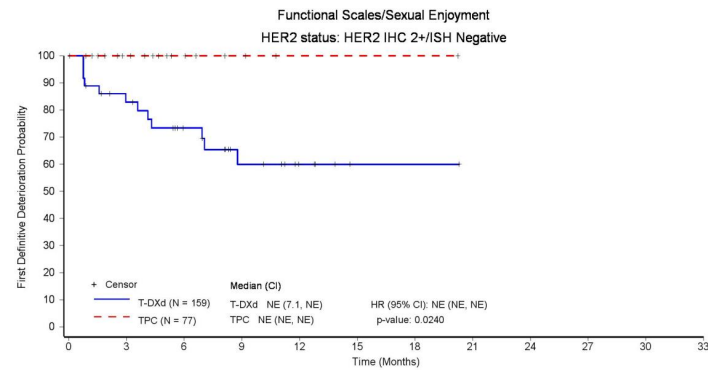
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:37; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F35BR45.rtf

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DE.F.7.4.4 - EORTC QLQ-BR45 - Definitive deterioration 10 Points - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO  
 11-Jan-2022 - Full Analysis Set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 159)	159	27	19	11	5	1	1	0	0	0	0	0
TPC (N = 77)	77	13	6	3	1	1	1	0	0	0	0	0

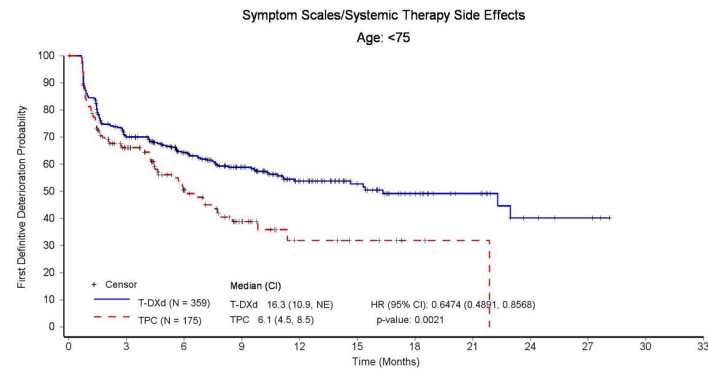
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:37; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F35BR45.rtf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 359)	359	219	163	122	77	47	28	16	5	3	0	0
TPC (N = 175)	175	84	42	19	7	5	2	1	0	0	0	0

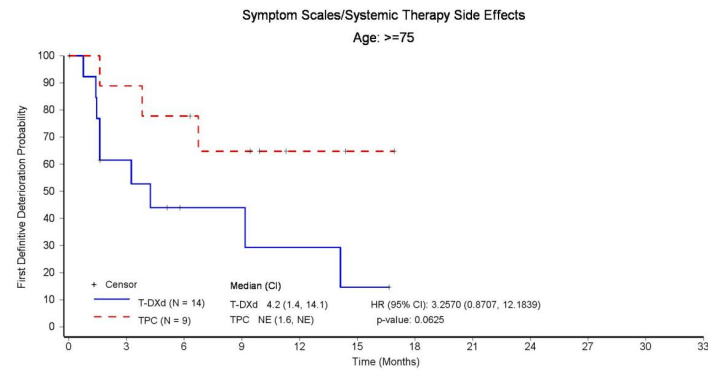
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:37; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F35BR45.rtf

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Patients still at risk:

T-DXd (N = 14)	14	7	3	3	2	1	0	0	0	0	0
TPC (N = 9)	9	8	7	5	2	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

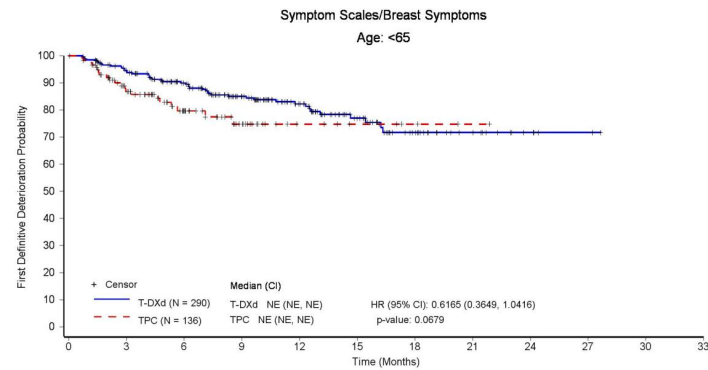
Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:37; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F35BR45.rtf



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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 290)	290	237	191	145	94	54	29	15	5	2	0	0
TPC (N = 136)	136	81	43	22	9	6	3	1	0	0	0	0

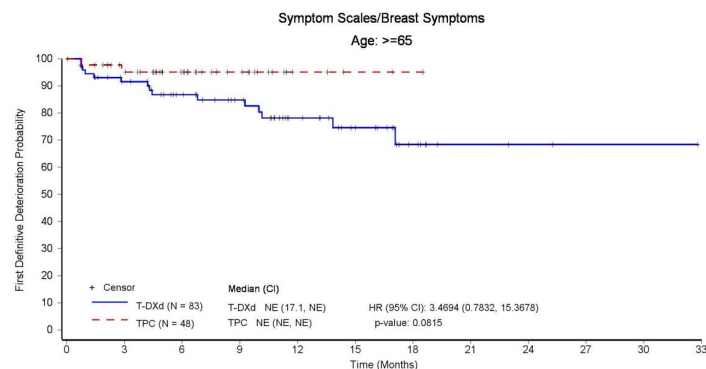
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:37; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F35BR45.rtf

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Patients still at risk:

T-DXd (N = 83)	83	60	48	39	26	18	8	3	2	1	1	0
TPC (N = 48)	48	36	24	14	4	2	1	0	0	0	0	0

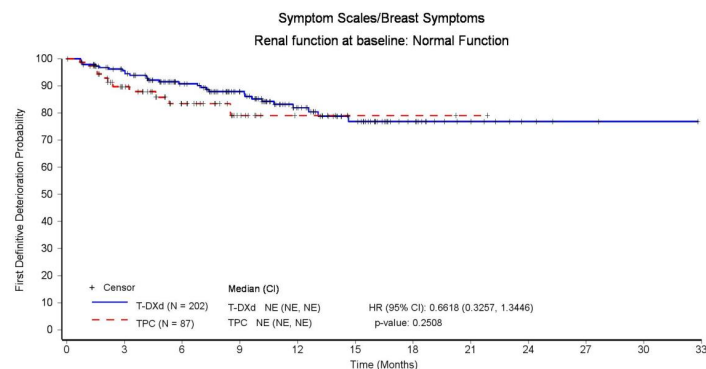
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:37; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F35BR45.rtf

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Patients still at risk:

T-DXd (N = 202)	202	167	130	101	60	39	20	10	4	2	1	0
TPC (N = 87)	87	52	29	13	6	2	2	1	0	0	0	0

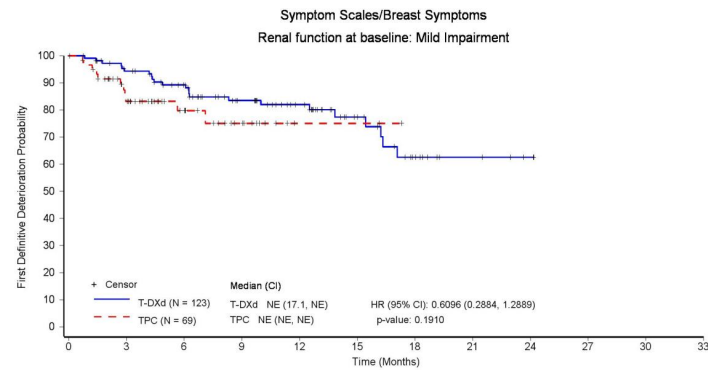
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:37; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F35BR45.rtf

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Patients still at risk:

T-DXd (N = 123)	123	97	82	61	46	24	12	6	2	0	0	0
TPC (N = 69)	69	40	22	11	2	2	0	0	0	0	0	0

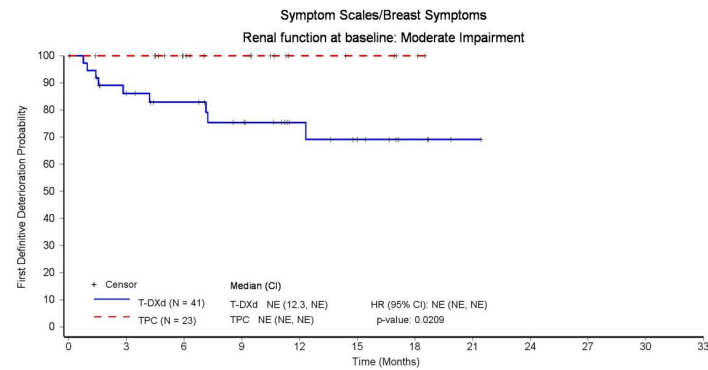
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:37; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F35BR45.rtf

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Patients still at risk:

T-DXd (N = 41)	41	28	24	19	12	8	4	1	0	0	0	0
TPC (N = 23)	23	21	14	11	5	4	2	0	0	0	0	0

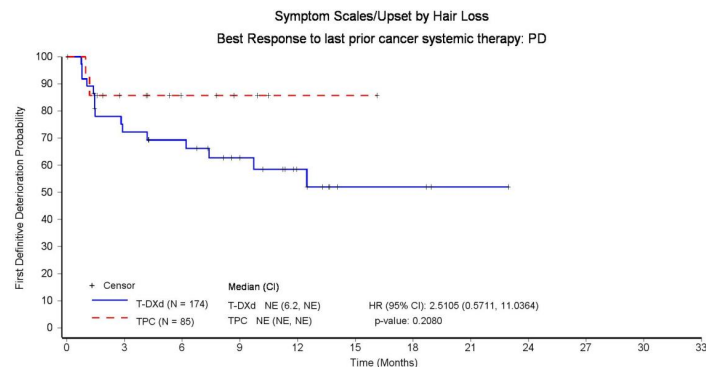
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:37; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F35BR45.rtf

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Patients still at risk:

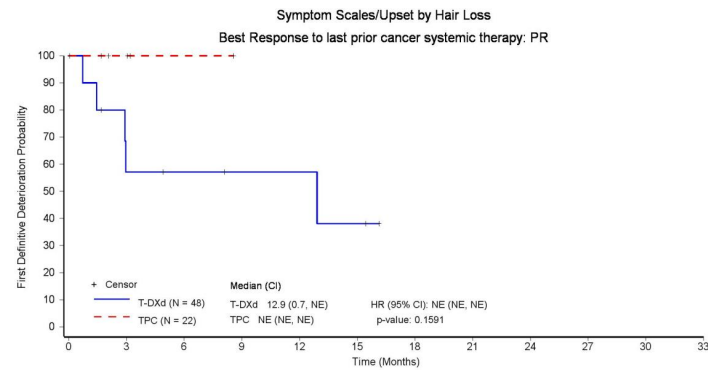
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 174)	174	25	22	16	9	3	3	1	0	0	0	0
TPC (N = 85)	85	9	5	3	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:37; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F35BR45.rtf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 48)	48	5	4	3	3	2	0	0	0	0	0	0
TPC (N = 22)	22	3	1	0	0	0	0	0	0	0	0	0

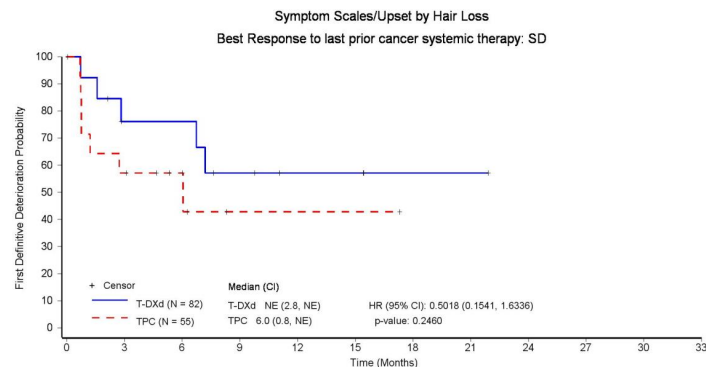
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:37; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F35BR45.rtf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 82)	82	8	8	5	3	3	1	1	0	0	0	0
TPC (N = 55)	55	8	5	1	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 10JAN2023 – 19:37; Program name: F3\_EQ5D\_FD\_4\_FAS.sas; Output name: F35BR45.rtf



**Anhang 4-G 3.6: Rücklauf**

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 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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 DE.T.3.13.1 - Questionnaire completion - Patients with baseline and at least one post-baseline measurement - Descriptive summary - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

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	T-DXd (N=373) n(%)	TPC (N=184) n(%)
Global Health Status	350(93.8)	164(89.1)
Functional Scales - Physical Functioning	351(94.1)	165(89.7)
Functional Scales - Role Functioning	351(94.1)	163(88.6)
Functional Scales - Emotional Functioning	351(94.1)	165(89.7)
Functional Scales - Cognitive Functioning	348(93.3)	163(88.6)
Functional Scales - Social Functioning	347(93.0)	165(89.7)
Symptom Scales - Fatigue	352(94.4)	164(89.1)
Symptom Scales - Nausea and Vomiting	352(94.4)	165(89.7)
Symptom Scales - Pain	348(93.3)	163(88.6)
Common Symptoms - Dyspnoea	352(94.4)	165(89.7)
Common Symptoms - Insomnia	352(94.4)	165(89.7)
Common Symptoms - Appetite Loss	352(94.4)	165(89.7)
Common Symptoms - Constipation	352(94.4)	165(89.7)

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 15SEP2022 – 12:23; Program name: T3\_QOL\_1\_FAS.sas; Output name: T3\_QOL\_1\_FAS.rtf

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DE.T.3.13.1 - Questionnaire completion - Patients with baseline and at least one post-baseline measurement - Descriptive summary - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

	T-DXd (N=373) n(%)	TPC (N=184) n(%)
Common Symptoms - Diarrhea	351(94.1)	165(89.7)
Common Symptoms - Financial Difficulties	348(93.3)	165(89.7)
Functional Scales - Body Image	347(93.0)	164(89.1)
Functional Scales - Sexual Functioning	342(91.7)	156(84.8)
Functional Scales - Sexual Enjoyment	68(18.2)	34(18.5)
Functional Scales - Future Perspective	348(93.3)	163(88.6)
Symptom Scales - Systemic Therapy Side Effects	350(93.8)	164(89.1)
Symptom Scales - Breast Symptoms	343(92.0)	163(88.6)
Symptom Scales - Arm Symptoms	350(93.8)	163(88.6)
Symptom Scales - Upset by Hair Loss	79(21.2)	35(19.0)
EQ-5D-5L VAS	346(92.8)	162(88.0)

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 15SEP2022 – 12:23; Program name: T3\_QOL\_1\_FAS.sas; Output name: T3\_QOL\_1\_FAS.rtf

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DE.T.3.13.2 - Questionnaire completion - Response rates - Descriptive summary - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Global Health Status	Baseline	373	360(96.5)	184	170(92.4)
	C2D1	373	333(89.3)	184	154(83.7)
	C3D1	368	317(86.1)	181	131(72.4)
	C5D1	365	278(76.2)	180	83(46.1)
	C7D1	357	254(71.1)	175	53(30.3)
	C9D1	350	215(61.4)	171	34(19.9)
	C11D1	344	186(54.1)	162	25(15.4)
	C13D1	331	147(44.4)	152	20(13.2)
	C15D1	319	130(40.8)	141	13(9.2)
	C17D1	307	102(33.2)	135	10(7.4)

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

[b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
Run date: 15SEP2022 – 12:23; Program name: T3\_QOL\_2\_FAS1.sas; Output name: T3\_QOL\_2\_FAS.rtf

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DE.T.3.13.2 - Questionnaire completion - Response rates - Descriptive summary - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Global Health Status	C19D1	298	88(29.5)	129	9(7.0)
	C21D1	278	72(25.9)	121	8(6.6)
	C23D1	238	58(24.4)	102	6(5.9)
	C25D1	206	48(23.3)	88	4(4.5)
	C27D1	170	37(21.8)	65	1(1.5)
	C29D1	129	26(20.2)	52	0
	C31D1	102	17(16.7)	42	0
	C33D1	86	15(17.4)	36	0
	C35D1	59	12(20.3)	26	0
C37D1	42	3(7.1)	19	0	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 15SEP2022 – 12:23; Program name: T3\_QOL\_2\_FAS1.sas; Output name: T3\_QOL\_2\_FAS.rtf

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Global Health Status	C39D1	24	3(12.5)	12	0
	C41D1	16	3(18.8)	7	0
	C43D1	11	1(9.1)	4	0
	C45D1	6	1(16.7)	1	0
	C47D1	1	1(100)	1	0
	C49D1	1	1(100)	0	0
	EOT	315	252(80.0)	181	133(73.5)
	40 Day Follow-Up	300	85(28.3)	175	59(33.7)
3 Months Follow-Up	245	139(56.7)	155	75(48.4)	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

[b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 15SEP2022 – 12:23; Program name: T3\_QOL\_2\_FAS1.sas; Output name: T3\_QOL\_2\_FAS.rtf

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Functional Scales - Physical Functioning	Baseline	373	361(96.8)	184	171(92.9)
	C2D1	373	334(89.5)	184	153(83.2)
	C3D1	368	320(87.0)	181	131(72.4)
	C5D1	365	279(76.4)	180	83(46.1)
	C7D1	357	256(71.7)	175	55(31.4)
	C9D1	350	217(62.0)	171	34(19.9)
	C11D1	344	187(54.4)	162	25(15.4)
	C13D1	331	148(44.7)	152	20(13.2)
	C15D1	319	131(41.1)	141	13(9.2)
	C17D1	307	103(33.6)	135	10(7.4)

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

[b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Run date: 15SEP2022 – 12:23; Program name: T3\_QOL\_2\_FAS1.sas; Output name: T3\_QOL\_2\_FAS.rtf

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Functional Scales - Physical Functioning	C19D1	298	90(30.2)	129	9(7.0)
	C21D1	278	73(26.3)	121	8(6.6)
	C23D1	238	58(24.4)	102	6(5.9)
	C25D1	206	48(23.3)	88	4(4.5)
	C27D1	170	37(21.8)	65	1(1.5)
	C29D1	129	26(20.2)	52	0
	C31D1	102	17(16.7)	42	0
	C33D1	86	15(17.4)	36	0
	C35D1	59	12(20.3)	26	0
C37D1	42	3(7.1)	19	0	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

[b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Run date: 15SEP2022 – 12:23; Program name: T3\_QOL\_2\_FAS1.sas; Output name: T3\_QOL\_2\_FAS.rtf



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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Functional Scales - Physical Functioning	C39D1	24	3(12.5)	12	0
	C41D1	16	3(18.8)	7	0
	C43D1	11	1(9.1)	4	0
	C45D1	6	1(16.7)	1	0
	C47D1	1	1(100)	1	0
	C49D1	1	1(100)	0	0
	EOT	315	254(80.6)	181	133(73.5)
	40 Day Follow-Up	300	89(29.7)	175	60(34.3)
3 Months Follow-Up	245	140(57.1)	155	76(49.0)	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

[b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Functional Scales - Role Functioning	Baseline	373	361(96.8)	184	169(91.8)
	C2D1	373	330(88.5)	184	153(83.2)
	C3D1	368	318(86.4)	181	131(72.4)
	C5D1	365	276(75.6)	180	82(45.6)
	C7D1	357	252(70.6)	175	55(31.4)
	C9D1	350	214(61.1)	171	34(19.9)
	C11D1	344	185(53.8)	162	25(15.4)
	C13D1	331	147(44.4)	152	20(13.2)
	C15D1	319	129(40.4)	141	13(9.2)
	C17D1	307	103(33.6)	135	10(7.4)

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

[b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Functional Scales - Role Functioning	C19D1	298	88(29.5)	129	9(7.0)
	C21D1	278	72(25.9)	121	8(6.6)
	C23D1	238	58(24.4)	102	6(5.9)
	C25D1	206	48(23.3)	88	4(4.5)
	C27D1	170	37(21.8)	65	1(1.5)
	C29D1	129	26(20.2)	52	0
	C31D1	102	17(16.7)	42	0
	C33D1	86	15(17.4)	36	0
	C35D1	59	12(20.3)	26	0
C37D1	42	3(7.1)	19	0	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

[b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Functional Scales - Role Functioning	C39D1	24	3(12.5)	12	0
	C41D1	16	3(18.8)	7	0
	C43D1	11	1(9.1)	4	0
	C45D1	6	1(16.7)	1	0
	C47D1	1	1(100)	1	0
	C49D1	1	1(100)	0	0
	EOT	315	253(80.3)	181	132(72.9)
	40 Day Follow-Up	300	88(29.3)	175	60(34.3)
3 Months Follow-Up	245	139(56.7)	155	73(47.1)	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

[b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Functional Scales - Emotional Functioning	Baseline	373	361(96.8)	184	171(92.9)
	C2D1	373	334(89.5)	184	154(83.7)
	C3D1	368	316(85.9)	181	132(72.9)
	C5D1	365	278(76.2)	180	83(46.1)
	C7D1	357	255(71.4)	175	52(29.7)
	C9D1	350	217(62.0)	171	34(19.9)
	C11D1	344	187(54.4)	162	25(15.4)
	C13D1	331	146(44.1)	152	20(13.2)
	C15D1	319	131(41.1)	141	13(9.2)
	C17D1	307	103(33.6)	135	10(7.4)

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Functional Scales - Emotional Functioning	C19D1	298	90(30.2)	129	9(7.0)
	C21D1	278	72(25.9)	121	8(6.6)
	C23D1	238	58(24.4)	102	6(5.9)
	C25D1	206	48(23.3)	88	4(4.5)
	C27D1	170	37(21.8)	65	1(1.5)
	C29D1	129	26(20.2)	52	0
	C31D1	102	17(16.7)	42	0
	C33D1	86	15(17.4)	36	0
	C35D1	59	12(20.3)	26	0
C37D1	42	3(7.1)	19	0	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

[b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Functional Scales - Emotional Functioning	C39D1	24	3(12.5)	12	0
	C41D1	16	3(18.8)	7	0
	C43D1	11	1(9.1)	4	0
	C45D1	6	1(16.7)	1	0
	C47D1	1	1(100)	1	0
	C49D1	1	1(100)	0	0
	EOT	315	253(80.3)	181	133(73.5)
	40 Day Follow-Up	300	86(28.7)	175	60(34.3)
3 Months Follow-Up	245	140(57.1)	155	74(47.7)	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Functional Scales - Cognitive Functioning	Baseline	373	358(96.0)	184	170(92.4)
	C2D1	373	333(89.3)	184	154(83.7)
	C3D1	368	312(84.8)	181	132(72.9)
	C5D1	365	277(75.9)	180	83(46.1)
	C7D1	357	252(70.6)	175	51(29.1)
	C9D1	350	216(61.7)	171	34(19.9)
	C11D1	344	186(54.1)	162	25(15.4)
	C13D1	331	146(44.1)	152	20(13.2)
	C15D1	319	130(40.8)	141	13(9.2)
	C17D1	307	101(32.9)	135	10(7.4)

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Functional Scales - Cognitive Functioning	C19D1	298	87(29.2)	129	9(7.0)
	C21D1	278	72(25.9)	121	8(6.6)
	C23D1	238	58(24.4)	102	6(5.9)
	C25D1	206	48(23.3)	88	4(4.5)
	C27D1	170	37(21.8)	65	1(1.5)
	C29D1	129	26(20.2)	52	0
	C31D1	102	17(16.7)	42	0
	C33D1	86	15(17.4)	36	0
	C35D1	59	12(20.3)	26	0
C37D1	42	3(7.1)	19	0	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

[b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Functional Scales - Cognitive Functioning	C39D1	24	3(12.5)	12	0
	C41D1	16	3(18.8)	7	0
	C43D1	11	1(9.1)	4	0
	C45D1	6	1(16.7)	1	0
	C47D1	1	1(100)	1	0
	C49D1	1	1(100)	0	0
	EOT	315	252(80.0)	181	132(72.9)
	40 Day Follow-Up	300	84(28.0)	175	60(34.3)
3 Months Follow-Up	245	139(56.7)	155	73(47.1)	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 15SEP2022 – 12:23; Program name: T3\_QOL\_2\_FAS1.sas; Output name: T3\_QOL\_2\_FAS.rtf

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Functional Scales - Social Functioning	Baseline	373	359(96.2)	184	171(92.9)
	C2D1	373	329(88.2)	184	154(83.7)
	C3D1	368	312(84.8)	181	132(72.9)
	C5D1	365	276(75.6)	180	83(46.1)
	C7D1	357	250(70.0)	175	52(29.7)
	C9D1	350	212(60.6)	171	34(19.9)
	C11D1	344	184(53.5)	162	25(15.4)
	C13D1	331	142(42.9)	152	20(13.2)
	C15D1	319	129(40.4)	141	13(9.2)
	C17D1	307	102(33.2)	135	10(7.4)

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Functional Scales - Social Functioning	C19D1	298	87(29.2)	129	9(7.0)
	C21D1	278	72(25.9)	121	8(6.6)
	C23D1	238	58(24.4)	102	6(5.9)
	C25D1	206	48(23.3)	88	4(4.5)
	C27D1	170	37(21.8)	65	1(1.5)
	C29D1	129	26(20.2)	52	0
	C31D1	102	17(16.7)	42	0
	C33D1	86	15(17.4)	36	0
	C35D1	59	12(20.3)	26	0
C37D1	42	3(7.1)	19	0	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Functional Scales - Social Functioning	C39D1	24	3(12.5)	12	0
	C41D1	16	3(18.8)	7	0
	C43D1	11	1(9.1)	4	0
	C45D1	6	1(16.7)	1	0
	C47D1	1	1(100)	1	0
	C49D1	1	1(100)	0	0
	EOT	315	251(79.7)	181	132(72.9)
	40 Day Follow-Up	300	86(28.7)	175	60(34.3)
3 Months Follow-Up	245	139(56.7)	155	74(47.7)	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

[b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Run date: 15SEP2022 – 12:23; Program name: T3\_QOL\_2\_FAS1.sas; Output name: T3\_QOL\_2\_FAS.rtf

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Symptom Scales - Fatigue	Baseline	373	362(97.1)	184	170(92.4)
	C2D1	373	333(89.3)	184	153(83.2)
	C3D1	368	321(87.2)	181	132(72.9)
	C5D1	365	278(76.2)	180	83(46.1)
	C7D1	357	256(71.7)	175	55(31.4)
	C9D1	350	217(62.0)	171	34(19.9)
	C11D1	344	188(54.7)	162	25(15.4)
	C13D1	331	148(44.7)	152	20(13.2)
	C15D1	319	131(41.1)	141	13(9.2)
	C17D1	307	102(33.2)	135	10(7.4)

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Symptom Scales - Fatigue	C19D1	298	90(30.2)	129	9(7.0)
	C21D1	278	73(26.3)	121	8(6.6)
	C23D1	238	58(24.4)	102	6(5.9)
	C25D1	206	48(23.3)	88	4(4.5)
	C27D1	170	37(21.8)	65	1(1.5)
	C29D1	129	26(20.2)	52	0
	C31D1	102	17(16.7)	42	0
	C33D1	86	15(17.4)	36	0
	C35D1	59	12(20.3)	26	0
C37D1	42	3(7.1)	19	0	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

[b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Symptom Scales - Fatigue	C39D1	24	3(12.5)	12	0
	C41D1	16	3(18.8)	7	0
	C43D1	11	1(9.1)	4	0
	C45D1	6	1(16.7)	1	0
	C47D1	1	1(100)	1	0
	C49D1	1	1(100)	0	0
	EOT	315	253(80.3)	181	133(73.5)
	40 Day Follow-Up	300	88(29.3)	175	60(34.3)
3 Months Follow-Up	245	140(57.1)	155	76(49.0)	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Symptom Scales - Nausea and Vomiting	Baseline	373	362(97.1)	184	171(92.9)
	C2D1	373	333(89.3)	184	152(82.6)
	C3D1	368	321(87.2)	181	132(72.9)
	C5D1	365	278(76.2)	180	83(46.1)
	C7D1	357	256(71.7)	175	55(31.4)
	C9D1	350	216(61.7)	171	34(19.9)
	C11D1	344	188(54.7)	162	25(15.4)
	C13D1	331	147(44.4)	152	20(13.2)
	C15D1	319	131(41.1)	141	13(9.2)
	C17D1	307	102(33.2)	135	10(7.4)

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Symptom Scales - Nausea and Vomiting	C19D1	298	90(30.2)	129	9(7.0)
	C21D1	278	73(26.3)	121	8(6.6)
	C23D1	238	58(24.4)	102	6(5.9)
	C25D1	206	48(23.3)	88	4(4.5)
	C27D1	170	37(21.8)	65	1(1.5)
	C29D1	129	26(20.2)	52	0
	C31D1	102	17(16.7)	42	0
	C33D1	86	15(17.4)	36	0
	C35D1	59	11(18.6)	26	0
C37D1	42	3(7.1)	19	0	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Symptom Scales - Nausea and Vomiting	C39D1	24	3(12.5)	12	0
	C41D1	16	3(18.8)	7	0
	C43D1	11	1(9.1)	4	0
	C45D1	6	1(16.7)	1	0
	C47D1	1	1(100)	1	0
	C49D1	1	1(100)	0	0
	EOT	315	252(80.0)	181	133(73.5)
	40 Day Follow-Up	300	88(29.3)	175	60(34.3)
3 Months Follow-Up	245	139(56.7)	155	76(49.0)	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Symptom Scales - Pain	Baseline	373	358(96.0)	184	170(92.4)
	C2D1	373	331(88.7)	184	152(82.6)
	C3D1	368	317(86.1)	181	131(72.4)
	C5D1	365	277(75.9)	180	83(46.1)
	C7D1	357	253(70.9)	175	53(30.3)
	C9D1	350	214(61.1)	171	34(19.9)
	C11D1	344	186(54.1)	162	25(15.4)
	C13D1	331	146(44.1)	152	20(13.2)
	C15D1	319	129(40.4)	141	13(9.2)
	C17D1	307	101(32.9)	135	10(7.4)

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

[b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Symptom Scales - Pain	C19D1	298	90(30.2)	129	9(7.0)
	C21D1	278	72(25.9)	121	8(6.6)
	C23D1	238	58(24.4)	102	6(5.9)
	C25D1	206	48(23.3)	88	4(4.5)
	C27D1	170	37(21.8)	65	1(1.5)
	C29D1	129	26(20.2)	52	0
	C31D1	102	17(16.7)	42	0
	C33D1	86	15(17.4)	36	0
	C35D1	59	11(18.6)	26	0
C37D1	42	3(7.1)	19	0	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Symptom Scales - Pain	C39D1	24	3(12.5)	12	0
	C41D1	16	3(18.8)	7	0
	C43D1	11	1(9.1)	4	0
	C45D1	6	1(16.7)	1	0
	C47D1	1	1(100)	1	0
	C49D1	1	1(100)	0	0
	EOT	315	252(80.0)	181	132(72.9)
	40 Day Follow-Up	300	87(29.0)	175	60(34.3)
3 Months Follow-Up	245	139(56.7)	155	75(48.4)	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Common Symptoms - Dyspnoea	Baseline	373	362(97.1)	184	171(92.9)
	C2D1	373	332(89.0)	184	153(83.2)
	C3D1	368	318(86.4)	181	131(72.4)
	C5D1	365	279(76.4)	180	83(46.1)
	C7D1	357	255(71.4)	175	55(31.4)
	C9D1	350	215(61.4)	171	34(19.9)
	C11D1	344	187(54.4)	162	25(15.4)
	C13D1	331	148(44.7)	152	20(13.2)
	C15D1	319	130(40.8)	141	13(9.2)
	C17D1	307	102(33.2)	135	10(7.4)

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

[b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Common Symptoms - Dyspnoea	C19D1	298	90(30.2)	129	9(7.0)
	C21D1	278	73(26.3)	121	8(6.6)
	C23D1	238	58(24.4)	102	6(5.9)
	C25D1	206	48(23.3)	88	4(4.5)
	C27D1	170	37(21.8)	65	1(1.5)
	C29D1	129	26(20.2)	52	0
	C31D1	102	17(16.7)	42	0
	C33D1	86	15(17.4)	36	0
	C35D1	59	12(20.3)	26	0
C37D1	42	3(7.1)	19	0	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Common Symptoms - Dyspnoea	C39D1	24	3(12.5)	12	0
	C41D1	16	3(18.8)	7	0
	C43D1	11	1(9.1)	4	0
	C45D1	6	1(16.7)	1	0
	C47D1	1	1(100)	1	0
	C49D1	1	1(100)	0	0
	EOT	315	253(80.3)	181	133(73.5)
	40 Day Follow-Up	300	88(29.3)	175	60(34.3)
3 Months Follow-Up	245	140(57.1)	155	76(49.0)	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Common Symptoms - Insomnia	Baseline	373	362(97.1)	184	171(92.9)
	C2D1	373	333(89.3)	184	153(83.2)
	C3D1	368	320(87.0)	181	132(72.9)
	C5D1	365	278(76.2)	180	83(46.1)
	C7D1	357	256(71.7)	175	54(30.9)
	C9D1	350	217(62.0)	171	34(19.9)
	C11D1	344	187(54.4)	162	25(15.4)
	C13D1	331	148(44.7)	152	20(13.2)
	C15D1	319	131(41.1)	141	13(9.2)
	C17D1	307	103(33.6)	135	10(7.4)

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Common Symptoms - Insomnia	C19D1	298	90(30.2)	129	9(7.0)
	C21D1	278	73(26.3)	121	8(6.6)
	C23D1	238	58(24.4)	102	6(5.9)
	C25D1	206	48(23.3)	88	4(4.5)
	C27D1	170	37(21.8)	65	1(1.5)
	C29D1	129	26(20.2)	52	0
	C31D1	102	17(16.7)	42	0
	C33D1	86	15(17.4)	36	0
	C35D1	59	12(20.3)	26	0
C37D1	42	3(7.1)	19	0	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Common Symptoms - Insomnia	C39D1	24	3(12.5)	12	0
	C41D1	16	3(18.8)	7	0
	C43D1	11	1(9.1)	4	0
	C45D1	6	1(16.7)	1	0
	C47D1	1	1(100)	1	0
	C49D1	1	1(100)	0	0
	EOT	315	253(80.3)	181	133(73.5)
	40 Day Follow-Up	300	88(29.3)	175	60(34.3)
3 Months Follow-Up	245	140(57.1)	155	76(49.0)	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Common Symptoms - Appetite Loss	Baseline	373	362(97.1)	184	171(92.9)
	C2D1	373	334(89.5)	184	153(83.2)
	C3D1	368	320(87.0)	181	132(72.9)
	C5D1	365	279(76.4)	180	83(46.1)
	C7D1	357	256(71.7)	175	55(31.4)
	C9D1	350	216(61.7)	171	34(19.9)
	C11D1	344	185(53.8)	162	25(15.4)
	C13D1	331	148(44.7)	152	20(13.2)
	C15D1	319	131(41.1)	141	13(9.2)
	C17D1	307	102(33.2)	135	10(7.4)

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

[b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Common Symptoms - Appetite Loss	C19D1	298	89(29.9)	129	9(7.0)
	C21D1	278	73(26.3)	121	8(6.6)
	C23D1	238	58(24.4)	102	6(5.9)
	C25D1	206	48(23.3)	88	4(4.5)
	C27D1	170	37(21.8)	65	1(1.5)
	C29D1	129	26(20.2)	52	0
	C31D1	102	17(16.7)	42	0
	C33D1	86	15(17.4)	36	0
	C35D1	59	12(20.3)	26	0
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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Common Symptoms - Appetite Loss	C39D1	24	3(12.5)	12	0
	C41D1	16	3(18.8)	7	0
	C43D1	11	1(9.1)	4	0
	C45D1	6	1(16.7)	1	0
	C47D1	1	1(100)	1	0
	C49D1	1	1(100)	0	0
	EOT	315	253(80.3)	181	133(73.5)
	40 Day Follow-Up	300	87(29.0)	175	60(34.3)
3 Months Follow-Up	245	140(57.1)	155	76(49.0)	

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Common Symptoms - Constipation	Baseline	373	362(97.1)	184	171(92.9)
	C2D1	373	333(89.3)	184	153(83.2)
	C3D1	368	320(87.0)	181	132(72.9)
	C5D1	365	278(76.2)	180	83(46.1)
	C7D1	357	255(71.4)	175	55(31.4)
	C9D1	350	217(62.0)	171	34(19.9)
	C11D1	344	186(54.1)	162	25(15.4)
	C13D1	331	148(44.7)	152	20(13.2)
	C15D1	319	131(41.1)	141	13(9.2)
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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Common Symptoms - Constipation	C19D1	298	90(30.2)	129	9(7.0)
	C21D1	278	73(26.3)	121	8(6.6)
	C23D1	238	58(24.4)	102	6(5.9)
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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Common Symptoms - Constipation	C39D1	24	3(12.5)	12	0
	C41D1	16	3(18.8)	7	0
	C43D1	11	1(9.1)	4	0
	C45D1	6	1(16.7)	1	0
	C47D1	1	1(100)	1	0
	C49D1	1	1(100)	0	0
	EOT	315	253(80.3)	181	133(73.5)
	40 Day Follow-Up	300	87(29.0)	175	60(34.3)
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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Common Symptoms - Diarrhea	Baseline	373	361(96.8)	184	171(92.9)
	C2D1	373	334(89.5)	184	153(83.2)
	C3D1	368	319(86.7)	181	132(72.9)
	C5D1	365	279(76.4)	180	83(46.1)
	C7D1	357	255(71.4)	175	54(30.9)
	C9D1	350	217(62.0)	171	34(19.9)
	C11D1	344	188(54.7)	162	25(15.4)
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	C15D1	319	131(41.1)	141	13(9.2)
	C17D1	307	102(33.2)	135	10(7.4)

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

[b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
Run date: 15SEP2022 – 12:23; Program name: T3\_QOL\_2\_FAS1.sas; Output name: T3\_QOL\_2\_FAS.rtf

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Common Symptoms - Diarrhea	C19D1	298	90(30.2)	129	9(7.0)
	C21D1	278	73(26.3)	121	8(6.6)
	C23D1	238	58(24.4)	102	6(5.9)
	C25D1	206	48(23.3)	88	4(4.5)
	C27D1	170	37(21.8)	65	1(1.5)
	C29D1	129	26(20.2)	52	0
	C31D1	102	17(16.7)	42	0
	C33D1	86	15(17.4)	36	0
	C35D1	59	12(20.3)	26	0
C37D1	42	3(7.1)	19	0	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 15SEP2022 – 12:23; Program name: T3\_QOL\_2\_FAS1.sas; Output name: T3\_QOL\_2\_FAS.rtf

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Common Symptoms - Diarrhea	C39D1	24	3(12.5)	12	0
	C41D1	16	3(18.8)	7	0
	C43D1	11	1(9.1)	4	0
	C45D1	6	1(16.7)	1	0
	C47D1	1	1(100)	1	0
	C49D1	1	1(100)	0	0
	EOT	315	252(80.0)	181	133(73.5)
	40 Day Follow-Up	300	87(29.0)	175	60(34.3)
3 Months Follow-Up	245	139(56.7)	155	76(49.0)	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

[b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 15SEP2022 – 12:23; Program name: T3\_QOL\_2\_FAS1.sas; Output name: T3\_QOL\_2\_FAS.rtf

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Common Symptoms - Financial Difficulties	Baseline	373	359(96.2)	184	171(92.9)
	C2D1	373	334(89.5)	184	154(83.7)
	C3D1	368	314(85.3)	181	132(72.9)
	C5D1	365	274(75.1)	180	83(46.1)
	C7D1	357	253(70.9)	175	52(29.7)
	C9D1	350	215(61.4)	171	34(19.9)
	C11D1	344	186(54.1)	162	25(15.4)
	C13D1	331	143(43.2)	152	20(13.2)
	C15D1	319	127(39.8)	141	13(9.2)
	C17D1	307	101(32.9)	135	10(7.4)

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

[b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Common Symptoms - Financial Difficulties	C19D1	298	88(29.5)	129	9(7.0)
	C21D1	278	72(25.9)	121	8(6.6)
	C23D1	238	58(24.4)	102	6(5.9)
	C25D1	206	48(23.3)	88	4(4.5)
	C27D1	170	37(21.8)	65	1(1.5)
	C29D1	129	26(20.2)	52	0
	C31D1	102	17(16.7)	42	0
	C33D1	86	15(17.4)	36	0
	C35D1	59	12(20.3)	26	0
C37D1	42	3(7.1)	19	0	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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 Run date: 15SEP2022 – 12:23; Program name: T3\_QOL\_2\_FAS1.sas; Output name: T3\_QOL\_2\_FAS.rtf

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Common Symptoms - Financial Difficulties	C39D1	24	3(12.5)	12	0
	C41D1	16	3(18.8)	7	0
	C43D1	11	1(9.1)	4	0
	C45D1	6	1(16.7)	1	0
	C47D1	1	1(100)	1	0
	C49D1	1	1(100)	0	0
	EOT	315	252(80.0)	181	133(73.5)
	40 Day Follow-Up	300	86(28.7)	175	60(34.3)
3 Months Follow-Up	245	140(57.1)	155	73(47.1)	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

[b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Functional Scales - Body Image	Baseline	373	357(95.7)	184	170(92.4)
	C2D1	373	334(89.5)	184	153(83.2)
	C3D1	368	318(86.4)	181	132(72.9)
	C5D1	365	276(75.6)	180	82(45.6)
	C7D1	357	253(70.9)	175	53(30.3)
	C9D1	350	211(60.3)	171	33(19.3)
	C11D1	344	186(54.1)	162	23(14.2)
	C13D1	331	145(43.8)	152	20(13.2)
	C15D1	319	130(40.8)	141	12(8.5)
	C17D1	307	101(32.9)	135	10(7.4)

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Functional Scales - Body Image	C19D1	298	89(29.9)	129	9(7.0)
	C21D1	278	73(26.3)	121	8(6.6)
	C23D1	238	58(24.4)	102	6(5.9)
	C25D1	206	48(23.3)	88	4(4.5)
	C27D1	170	37(21.8)	65	1(1.5)
	C29D1	129	26(20.2)	52	0
	C31D1	102	17(16.7)	42	0
	C33D1	86	15(17.4)	36	0
	C35D1	59	12(20.3)	26	0
C37D1	42	3(7.1)	19	0	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Functional Scales - Body Image	C39D1	24	3(12.5)	12	0
	C41D1	16	3(18.8)	7	0
	C43D1	11	1(9.1)	4	0
	C45D1	6	1(16.7)	1	0
	C47D1	1	1(100)	1	0
	C49D1	1	1(100)	0	0
	EOT	315	249(79.0)	181	133(73.5)
	40 Day Follow-Up	300	87(29.0)	175	60(34.3)
3 Months Follow-Up	245	136(55.5)	155	74(47.7)	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Functional Scales - Sexual Functioning	Baseline	373	355(95.2)	184	164(89.1)
	C2D1	373	324(86.9)	184	147(79.9)
	C3D1	368	307(83.4)	181	122(67.4)
	C5D1	365	266(72.9)	180	77(42.8)
	C7D1	357	243(68.1)	175	50(28.6)
	C9D1	350	199(56.9)	171	30(17.5)
	C11D1	344	173(50.3)	162	21(13.0)
	C13D1	331	134(40.5)	152	15(9.9)
	C15D1	319	119(37.3)	141	11(7.8)
	C17D1	307	91(29.6)	135	8(5.9)

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Functional Scales - Sexual Functioning	C19D1	298	81(27.2)	129	8(6.2)
	C21D1	278	69(24.8)	121	7(5.8)
	C23D1	238	53(22.3)	102	6(5.9)
	C25D1	206	46(22.3)	88	4(4.5)
	C27D1	170	35(20.6)	65	1(1.5)
	C29D1	129	24(18.6)	52	0
	C31D1	102	17(16.7)	42	0
	C33D1	86	15(17.4)	36	0
	C35D1	59	11(18.6)	26	0
C37D1	42	3(7.1)	19	0	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

[b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Functional Scales - Sexual Functioning	C39D1	24	3(12.5)	12	0
	C41D1	16	3(18.8)	7	0
	C43D1	11	1(9.1)	4	0
	C45D1	6	1(16.7)	1	0
	C47D1	1	1(100)	1	0
	C49D1	1	1(100)	0	0
	EOT	315	240(76.2)	181	124(68.5)
	40 Day Follow-Up	300	81(27.0)	175	57(32.6)
3 Months Follow-Up	245	129(52.7)	155	70(45.2)	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Functional Scales - Sexual Enjoyment	Baseline	373	82(22.0)	184	40(21.7)
	C2D1	373	64(17.2)	184	32(17.4)
	C3D1	368	62(16.8)	181	28(15.5)
	C5D1	365	58(15.9)	180	15(8.3)
	C7D1	357	50(14.0)	175	6(3.4)
	C9D1	350	41(11.7)	171	4(2.3)
	C11D1	344	30(8.7)	162	4(2.5)
	C13D1	331	31(9.4)	152	3(2.0)
	C15D1	319	25(7.8)	141	1(0.7)
	C17D1	307	18(5.9)	135	1(0.7)

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Functional Scales - Sexual Enjoyment	C19D1	298	15(5.0)	129	1(0.8)
	C21D1	278	16(5.8)	121	1(0.8)
	C23D1	238	11(4.6)	102	1(1.0)
	C25D1	206	12(5.8)	88	1(1.1)
	C27D1	170	6(3.5)	65	0
	C29D1	129	4(3.1)	52	0
	C31D1	102	3(2.9)	42	0
	C33D1	86	2(2.3)	36	0
	C35D1	59	2(3.4)	26	0
C37D1	42	0	19	0	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 15SEP2022 – 12:23; Program name: T3\_QOL\_2\_FAS1.sas; Output name: T3\_QOL\_2\_FAS.rtf



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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Functional Scales - Sexual Enjoyment	C39D1	24	1(4.2)	12	0
	C41D1	16	1(6.3)	7	0
	C43D1	11	0	4	0
	C45D1	6	0	1	0
	C47D1	1	0	1	0
	C49D1	1	0	0	0
	EOT	315	38(12.1)	181	25(13.8)
	40 Day Follow-Up	300	13(4.3)	175	10(5.7)
3 Months Follow-Up	245	20(8.2)	155	6(3.9)	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

[b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Functional Scales - Future Perspective	Baseline	373	358(96.0)	184	169(91.8)
	C2D1	373	333(89.3)	184	154(83.7)
	C3D1	368	320(87.0)	181	132(72.9)
	C5D1	365	278(76.2)	180	83(46.1)
	C7D1	357	253(70.9)	175	54(30.9)
	C9D1	350	214(61.1)	171	34(19.9)
	C11D1	344	187(54.4)	162	24(14.8)
	C13D1	331	144(43.5)	152	20(13.2)
	C15D1	319	130(40.8)	141	13(9.2)
	C17D1	307	101(32.9)	135	10(7.4)

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Functional Scales - Future Perspective	C19D1	298	89(29.9)	129	9(7.0)
	C21D1	278	74(26.6)	121	8(6.6)
	C23D1	238	58(24.4)	102	6(5.9)
	C25D1	206	48(23.3)	88	4(4.5)
	C27D1	170	37(21.8)	65	1(1.5)
	C29D1	129	26(20.2)	52	0
	C31D1	102	17(16.7)	42	0
	C33D1	86	15(17.4)	36	0
	C35D1	59	12(20.3)	26	0
C37D1	42	3(7.1)	19	0	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

[b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Functional Scales - Future Perspective	C39D1	24	3(12.5)	12	0
	C41D1	16	3(18.8)	7	0
	C43D1	11	1(9.1)	4	0
	C45D1	6	1(16.7)	1	0
	C47D1	1	1(100)	1	0
	C49D1	1	1(100)	0	0
	EOT	315	250(79.4)	181	133(73.5)
	40 Day Follow-Up	300	88(29.3)	175	59(33.7)
3 Months Follow-Up	245	138(56.3)	155	75(48.4)	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

[b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Run date: 15SEP2022 – 12:23; Program name: T3\_QOL\_2\_FAS1.sas; Output name: T3\_QOL\_2\_FAS.rtf

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Symptom Scales - Systemic Therapy Side Effects	Baseline	373	360(96.5)	184	170(92.4)
	C2D1	373	337(90.3)	184	154(83.7)
	C3D1	368	322(87.5)	181	132(72.9)
	C5D1	365	279(76.4)	180	83(46.1)
	C7D1	357	257(72.0)	175	54(30.9)
	C9D1	350	215(61.4)	171	34(19.9)
	C11D1	344	187(54.4)	162	24(14.8)
	C13D1	331	146(44.1)	152	20(13.2)
	C15D1	319	131(41.1)	141	13(9.2)
	C17D1	307	102(33.2)	135	10(7.4)

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

[b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Symptom Scales - Systemic Therapy Side Effects	C19D1	298	90(30.2)	129	9(7.0)
	C21D1	278	74(26.6)	121	8(6.6)
	C23D1	238	58(24.4)	102	6(5.9)
	C25D1	206	48(23.3)	88	4(4.5)
	C27D1	170	37(21.8)	65	1(1.5)
	C29D1	129	26(20.2)	52	0
	C31D1	102	17(16.7)	42	0
	C33D1	86	15(17.4)	36	0
	C35D1	59	12(20.3)	26	0
C37D1	42	3(7.1)	19	0	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Symptom Scales - Systemic Therapy Side Effects	C39D1	24	3(12.5)	12	0
	C41D1	16	3(18.8)	7	0
	C43D1	11	1(9.1)	4	0
	C45D1	6	1(16.7)	1	0
	C47D1	1	1(100)	1	0
	C49D1	1	1(100)	0	0
	EOT	315	255(81.0)	181	133(73.5)
	40 Day Follow-Up	300	89(29.7)	175	60(34.3)
3 Months Follow-Up	245	140(57.1)	155	76(49.0)	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Symptom Scales - Breast Symptoms	Baseline	373	353(94.6)	184	169(91.8)
	C2D1	373	333(89.3)	184	152(82.6)
	C3D1	368	316(85.9)	181	132(72.9)
	C5D1	365	273(74.8)	180	82(45.6)
	C7D1	357	250(70.0)	175	53(30.3)
	C9D1	350	211(60.3)	171	34(19.9)
	C11D1	344	183(53.2)	162	24(14.8)
	C13D1	331	142(42.9)	152	18(11.8)
	C15D1	319	129(40.4)	141	13(9.2)
	C17D1	307	96(31.3)	135	9(6.7)

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

[b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Symptom Scales - Breast Symptoms	C19D1	298	86(28.9)	129	9(7.0)
	C21D1	278	73(26.3)	121	8(6.6)
	C23D1	238	56(23.5)	102	6(5.9)
	C25D1	206	47(22.8)	88	4(4.5)
	C27D1	170	37(21.8)	65	1(1.5)
	C29D1	129	25(19.4)	52	0
	C31D1	102	16(15.7)	42	0
	C33D1	86	15(17.4)	36	0
	C35D1	59	12(20.3)	26	0
C37D1	42	3(7.1)	19	0	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

[b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Symptom Scales - Breast Symptoms	C39D1	24	3(12.5)	12	0
	C41D1	16	3(18.8)	7	0
	C43D1	11	1(9.1)	4	0
	C45D1	6	1(16.7)	1	0
	C47D1	1	1(100)	1	0
	C49D1	1	1(100)	0	0
	EOT	315	252(80.0)	181	133(73.5)
	40 Day Follow-Up	300	89(29.7)	175	59(33.7)
3 Months Follow-Up	245	138(56.3)	155	76(49.0)	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Symptom Scales - Arm Symptoms	Baseline	373	360(96.5)	184	169(91.8)
	C2D1	373	336(90.1)	184	153(83.2)
	C3D1	368	322(87.5)	181	132(72.9)
	C5D1	365	278(76.2)	180	83(46.1)
	C7D1	357	254(71.1)	175	54(30.9)
	C9D1	350	213(60.9)	171	34(19.9)
	C11D1	344	186(54.1)	162	25(15.4)
	C13D1	331	146(44.1)	152	20(13.2)
	C15D1	319	131(41.1)	141	13(9.2)
	C17D1	307	100(32.6)	135	10(7.4)

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Symptom Scales - Arm Symptoms	C19D1	298	89(29.9)	129	9(7.0)
	C21D1	278	73(26.3)	121	8(6.6)
	C23D1	238	58(24.4)	102	6(5.9)
	C25D1	206	46(22.3)	88	4(4.5)
	C27D1	170	37(21.8)	65	1(1.5)
	C29D1	129	26(20.2)	52	0
	C31D1	102	17(16.7)	42	0
	C33D1	86	15(17.4)	36	0
	C35D1	59	12(20.3)	26	0
C37D1	42	3(7.1)	19	0	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 15SEP2022 – 12:23; Program name: T3\_QOL\_2\_FAS1.sas; Output name: T3\_QOL\_2\_FAS.rtf

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Symptom Scales - Arm Symptoms	C39D1	24	3(12.5)	12	0
	C41D1	16	3(18.8)	7	0
	C43D1	11	1(9.1)	4	0
	C45D1	6	1(16.7)	1	0
	C47D1	1	1(100)	1	0
	C49D1	1	1(100)	0	0
	EOT	315	252(80.0)	181	133(73.5)
	40 Day Follow-Up	300	89(29.7)	175	60(34.3)
3 Months Follow-Up	245	140(57.1)	155	76(49.0)	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Symptom Scales - Upset by Hair Loss	Baseline	373	85(22.8)	184	47(25.5)
	C2D1	373	158(42.4)	184	94(51.1)
	C3D1	368	231(62.8)	181	78(43.1)
	C5D1	365	192(52.6)	180	45(25.0)
	C7D1	357	173(48.5)	175	28(16.0)
	C9D1	350	131(37.4)	171	18(10.5)
	C11D1	344	108(31.4)	162	9(5.6)
	C13D1	331	72(21.8)	152	8(5.3)
	C15D1	319	68(21.3)	141	5(3.5)
	C17D1	307	46(15.0)	135	4(3.0)

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

[b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Symptom Scales - Upset by Hair Loss	C19D1	298	45(15.1)	129	4(3.1)
	C21D1	278	35(12.6)	121	3(2.5)
	C23D1	238	27(11.3)	102	4(3.9)
	C25D1	206	20(9.7)	88	1(1.1)
	C27D1	170	17(10.0)	65	0
	C29D1	129	9(7.0)	52	0
	C31D1	102	9(8.8)	42	0
	C33D1	86	8(9.3)	36	0
	C35D1	59	7(11.9)	26	0
C37D1	42	0	19	0	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
Symptom Scales - Upset by Hair Loss	C39D1	24	1(4.2)	12	0
	C41D1	16	0	7	0
	C43D1	11	0	4	0
	C45D1	6	0	1	0
	C47D1	1	0	1	0
	C49D1	1	0	0	0
	EOT	315	125(39.7)	181	67(37.0)
	40 Day Follow-Up	300	54(18.0)	175	26(14.9)
3 Months Follow-Up	245	66(26.9)	155	32(20.6)	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

[b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Run date: 15SEP2022 – 12:23; Program name: T3\_QOL\_2\_FAS1.sas; Output name: T3\_QOL\_2\_FAS.rtf



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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
EQ-5D-5L VAS	Baseline	373	355(95.2)	184	169(91.8)
	C2D1	373	332(89.0)	184	153(83.2)
	C3D1	368	321(87.2)	181	131(72.4)
	C5D1	365	278(76.2)	180	79(43.9)
	C7D1	357	252(70.6)	175	55(31.4)
	C9D1	350	214(61.1)	171	34(19.9)
	C11D1	344	185(53.8)	162	25(15.4)
	C13D1	331	145(43.8)	152	20(13.2)
	C15D1	319	129(40.4)	141	13(9.2)
	C17D1	307	102(33.2)	135	10(7.4)

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

[b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
EQ-5D-5L VAS	C19D1	298	89(29.9)	129	9(7.0)
	C21D1	278	73(26.3)	121	8(6.6)
	C23D1	238	58(24.4)	102	6(5.9)
	C25D1	206	48(23.3)	88	4(4.5)
	C27D1	170	37(21.8)	65	1(1.5)
	C29D1	129	27(20.9)	52	0
	C31D1	102	17(16.7)	42	0
	C33D1	86	15(17.4)	36	0
	C35D1	59	11(18.6)	26	0
	C37D1	42	3(7.1)	19	0

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

[b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Questionnaire - Endpoint	Visit [a]	T-DXd (N=373)		TPC (N=184)	
		Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)	Number of subjects alive [b]	Number of subjects with completed questionnaires n (%)
EQ-5D-5L VAS	C39D1	24	3(12.5)	12	0
	C41D1	16	3(18.8)	7	0
	C43D1	11	1(9.1)	4	0
	C45D1	6	1(16.7)	1	0
	C47D1	1	1(100)	1	0
	C49D1	1	1(100)	0	0
	EOT	315	252(80.0)	181	130(71.8)
	40 Day Follow-Up	300	88(29.3)	175	60(34.3)
3 Months Follow-Up	245	139(56.7)	155	76(49.0)	

N: number of subjects in analysis set; % proportion of number of subjects alive (i.e. response rate); EOT: end of treatment.

[a] Visit is based on the window rules specified in study SAP

[b] Subjects defined as alive at the respective timepoint if minimum(death date, data cutoff date) – randomization date + 1 >= study day corresponding to the opening of respective visit window. For EOT, 40 Day Follow-Up, and 3 Months Follow-Up visits, subjects that were ongoing on study treatment at data cutoff date are excluded as they are not eligible for this visit.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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**Anhang 4-G 4: Ergänzende Analysen DESTINY-Breast04: Sicherheit**

**Anhang 4-G 4.1: Gesamtraten unerwünschter Ereignisse**

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DE.T.4.1.1 - Treatment-emergent adverse events - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	369 (99.5)	169 (98.3)	
Number of subjects censored, n (%)	2 (0.5)	3 (1.7)	
Median time to first event (months) [a]	0.1	0.1	
95% Confidence Interval	[NE, NE]	[0.1, 0.1]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			1.2098
95% Confidence Interval			[1.0005, 1.4628]
p-value			0.0494
Stratified log-rank p-value [c]			0.0504

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.1.2 - Treatment-emergent adverse events - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
HER2 status											0.9541
HER2 IHC 1+	214	213 (99.5)	1 (0.5)	0.1 (NE, NE)	100	97 (97.0)	3 (3.0)	0.1 (0.0, 0.1)	1.1706 (0.9179, 1.4928) 0.2042	0.1959	
HER2 IHC 2+/ISH Negative	157	156 (99.4)	1 (0.6)	0.1 (0.1, 0.1)	72	72 (100)	0	0.1 (0.1, 0.2)	1.1576 (0.8731, 1.5348) 0.3093	0.3032	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.1.2 - Treatment-emergent adverse events - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Number of prior lines of chemotherapy in a metastatic setting										0.6927
1	220	219 (99.5)	1 (0.5)	0.1 (0.1, 0.1)	94	92 (97.9)	2 (2.1)	0.1 (0.1, 0.2)	1.2114 (0.9476, 1.5487)	0.1265
>=2	150	149 (99.3)	1 (0.7)	0.1 (NE, NE)	78	77 (98.7)	1 (1.3)	0.1 (0.0, 0.1)	1.1032 (0.8345, 1.4585)	0.4743

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.1.2 - Treatment-emergent adverse events - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Prior CDK4/6											0.8375
Yes	233	231 (99.1)	2 (0.9)	0.1 (0.1, 0.1)	112	109 (97.3)	3 (2.7)	0.1 (0.1, 0.1)	1.1516 (0.9153, 1.4489) 0.2283	0.2238	
No	98	98 (100)	0	0.1 (0.1, 0.1)	43	43 (100)	0	0.1 (0.0, 0.3)	1.1982 (0.8309, 1.7278) 0.3330	0.3796	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7199
<65	289	287 (99.3)	2 (0.7)	0.1 (NE, NE)	126	123 (97.6)	3 (2.4)	0.1 (0.1, 0.2)	1.1902 (0.9615, 1.4733) 0.1098	0.1044	
>=65	82	82 (100)	0	0.1 (0.1, 0.1)	46	46 (100)	0	0.1 (0.0, 0.1)	1.0900 (0.7550, 1.5738) 0.6455	0.6102	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											0.6757
<75	357	355 (99.4)	2 (0.6)	0.1 (NE, NE)	163	160 (98.2)	3 (1.8)	0.1 (0.1, 0.1)	1.1398 (0.9441, 1.3761) 0.1735	0.1605	
>=75	14	14 (100)	0	0.2 (0.0, 0.5)	9	9 (100)	0	0.4 (0.0, 0.7)	1.3627 (0.5629, 3.2987) 0.4927	0.4741	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Race											0.6546
White	175	173 (98.9)	2 (1.1)	0.1 (0.1, 0.1)	85	82 (96.5)	3 (3.5)	0.1 (0.1, 0.2)	1.1980 (0.9190, 1.5616) 0.1816	0.1772	
Non-White	196	196 (100)	0	0.1 (NE, NE)	86	86 (100)	0	0.1 (0.0, 0.1)	1.1262 (0.8705, 1.4572) 0.3657	0.3651	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Region											0.6372
Asia	147	147 (100)	0	0.1 (NE, NE)	63	63 (100)	0	0.1 (0.0, 0.1)	1.0545 (0.7819, 1.4222) 0.7278	0.8011	
North America	58	58 (100)	0	0.1 (0.0, 0.1)	28	27 (96.4)	1 (3.6)	0.1 (0.0, 0.2)	1.0830 (0.6805, 1.7237) 0.7365	0.6744	
Europe + Israel	166	164 (98.8)	2 (1.2)	0.1 (0.1, 0.1)	81	79 (97.5)	2 (2.5)	0.1 (0.1, 0.2)	1.2451 (0.9498, 1.6322) 0.1124	0.1266	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
ECOG PS											0.6119
0	199	197 (99.0)	2 (1.0)	0.1 (NE, NE)	95	92 (96.8)	3 (3.2)	0.1 (0.1, 0.2)	1.1078 (0.8631, 1.4220) 0.4215	0.4376	
1	172	172 (100)	0	0.1 (0.1, 0.1)	77	77 (100)	0	0.1 (0.1, 0.1)	1.2345 (0.9401, 1.6211) 0.1296	0.1168	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.5353
0	60	60 (100)	0	0.1 (0.0, 0.1)	31	30 (96.8)	1 (3.2)	0.1 (0.0, 0.1)	0.8870 (0.5677, 1.3860) 0.5986	0.5542	
1	107	106 (99.1)	1 (0.9)	0.1 (0.1, 0.1)	48	47 (97.9)	1 (2.1)	0.1 (0.0, 0.2)	1.3617 (0.9598, 1.9319) 0.0836	0.0709	
2	114	113 (99.1)	1 (0.9)	0.1 (0.1, 0.1)	50	49 (98.0)	1 (2.0)	0.1 (0.1, 0.2)	1.2335 (0.8775, 1.7339) 0.2272	0.2355	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	90 (100)	0	0.1 (0.1, 0.1)	43	43 (100)	0	0.1 (0.1, 0.2)	1.1630 (0.8037, 1.6830) 0.4232	0.4472	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.5536
PD	173	171 (98.8)	2 (1.2)	0.1 (0.1, 0.1)	77	75 (97.4)	2 (2.6)	0.1 (0.1, 0.1)	1.0244 (0.7783, 1.3483) 0.8635	0.8440	
PR	48	48 (100)	0	0.1 (0.1, 0.1)	21	21 (100)	0	0.1 (0.0, 0.1)	1.1767 (0.6952, 1.9915) 0.5445	0.5288	
SD	82	82 (100)	0	0.1 (0.1, 0.1)	54	53 (98.1)	1 (1.9)	0.1 (0.1, 0.2)	1.3267 (0.9334, 1.8857) 0.1150	0.1125	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Reported history of CNS metastases											0.7771
Yes	37	37 (100)	0	0.1 (0.1, 0.1)	13	13 (100)	0	0.1 (0.0, 0.3)	1.0709 (0.5560, 2.0628) 0.8378	0.6417	
No	334	332 (99.4)	2 (0.6)	0.1 (NE, NE)	159	156 (98.1)	3 (1.9)	0.1 (0.1, 0.1)	1.1576 (0.9554, 1.4025) 0.1351	0.1298	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Baseline CNS metastases											0.3977
Yes	24	24 (100)	0	0.1 (0.0, 0.2)	7	7 (100)	0	0.1 (0.0, 0.3)	0.8259 (0.3417, 1.9966) 0.6711	0.6984	
No	347	345 (99.4)	2 (0.6)	0.1 (NE, NE)	165	162 (98.2)	3 (1.8)	0.1 (0.1, 0.1)	1.1801 (0.9774, 1.4248) 0.0850	0.0791	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Renal function at baseline											0.2334
Normal Function	201	200 (99.5)	1 (0.5)	0.1 (0.1, 0.1)	80	79 (98.8)	1 (1.3)	0.1 (0.0, 0.1)	1.0358 (0.7960, 1.3478) 0.7937	0.7017	
Mild Impairment	123	122 (99.2)	1 (0.8)	0.1 (0.0, 0.1)	65	63 (96.9)	2 (3.1)	0.1 (0.1, 0.2)	1.4326 (1.0507, 1.9533) 0.0230	0.0285	
Moderate Impairment	41	41 (100)	0	0.1 (0.1, 0.2)	23	23 (100)	0	0.1 (0.0, 0.3)	1.1139 (0.6510, 1.9057) 0.6939	0.7088	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hepatic function at baseline											0.7332
Normal Function	170	168 (98.8)	2 (1.2)	0.1 (0.1, 0.1)	88	88 (100)	0	0.1 (0.1, 0.1)	1.0916 (0.8414, 1.4161) 0.5094	0.5403	
Mild Impairment	194	194 (100)	0	0.1 (NE, NE)	82	79 (96.3)	3 (3.7)	0.1 (0.0, 0.2)	1.1873 (0.9116, 1.5463) 0.2028	0.1770	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Baseline visceral disease											0.7176
Yes	331	330 (99.7)	1 (0.3)	0.1 (NE, NE)	146	144 (98.6)	2 (1.4)	0.1 (0.1, 0.1)	1.1803 (0.9686, 1.4383) 0.1003	0.0961	
No	40	39 (97.5)	1 (2.5)	0.1 (0.0, 0.1)	26	25 (96.2)	1 (3.8)	0.1 (0.0, 0.1)	0.9970 (0.6003, 1.6561) 0.9908	0.9940	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.1.2 - Treatment-emergent adverse events - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (IXRS)											0.5357
Positive	329	327 (99.4)	2 (0.6)	0.1 (NE, NE)	152	149 (98.0)	3 (2.0)	0.1 (0.1, 0.1)	1.1818 (0.9720, 1.4368) 0.0940	0.0905	
Negative	42	42 (100)	0	0.1 (0.0, 0.1)	20	20 (100)	0	0.1 (0.0, 0.2)	0.9440 (0.5447, 1.6359) 0.8371	0.8220	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.1.2 - Treatment-emergent adverse events - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (derived)											0.8414
Positive	331	329 (99.4)	2 (0.6)	0.1 (NE, NE)	155	152 (98.1)	3 (1.9)	0.1 (0.1, 0.1)	1.1666 (0.9610, 1.4162) 0.1193	0.1177	
Negative	40	40 (100)	0	0.1 (0.0, 0.1)	17	17 (100)	0	0.1 (0.0, 0.3)	1.0372 (0.5769, 1.8646) 0.9030	0.8878	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

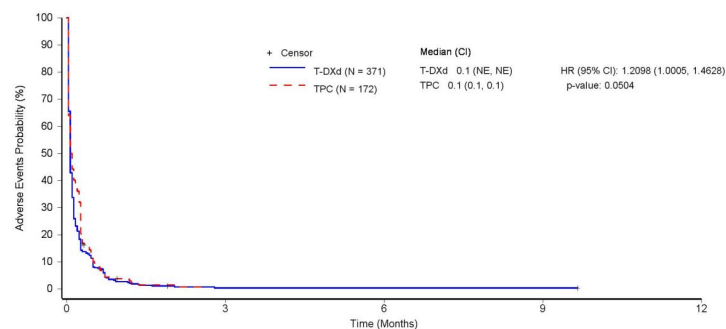
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.F.4.1.3 - Treatment-emergent adverse events - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:					
T-DXd (N = 371)	371	1	1	1	0
TPC (N = 172)	172	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

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 Run date: 21OCT2022 – 17:11; Program name: F4\_TEAE\_3\_SAS.sas; Output name: F4\_TEAE\_3\_SAS.rtf



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DE.F.4.1.4 - Treatment-emergent adverse events - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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No significant interaction has been found

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Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
Run date: 21OCT2022 – 17:11; Program name: F4\_TEAE\_4\_SAS.sas; Output name: F4\_TEAE\_4\_SAS.rtf

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DE.T.4.2.1 - Serious Treatment-emergent adverse events - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	103 (27.8)	43 (25.0)	
Number of subjects censored, n (%)	268 (72.2)	129 (75.0)	
Median time to first event (months) [a]	NE	NE	
95% Confidence Interval	[24.4, NE]	[9.2, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.6950
95% Confidence Interval			[0.4807, 1.0049]
p-value			0.0531
Stratified log-rank p-value [c]			0.0537

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.2.2 - Serious Treatment-emergent adverse events - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.7216
HER2 IHC 1+	214	56 (26.2)	158 (73.8)	NE (18.1, NE)	100	22 (22.0)	78 (78.0)	NE (7.2, NE)	0.7859 (0.4744, 1.3017) 0.3493	0.3552
HER2 IHC 2+/ISH Negative	157	47 (29.9)	110 (70.1)	24.4 (24.4, NE)	72	21 (29.2)	51 (70.8)	12.6 (9.2, NE)	0.6367 (0.3755, 1.0796) 0.0938	0.0922

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.2586
1	220	48 (21.8)	172 (78.2)	NE (24.4, NE)	94	23 (24.5)	71 (75.5)	12.6 (9.2, NE)	0.5837 (0.3507, 0.9716)	0.0370
>=2	150	55 (36.7)	95 (63.3)	NE (11.1, NE)	78	20 (25.6)	58 (74.4)	NE (5.5, NE)	0.8750 (0.5166, 1.4819)	0.6207

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Prior CDK4/6										0.9165
Yes	233	61 (26.2)	172 (73.8)	24.4 (24.4, NE)	112	26 (23.2)	86 (76.8)	12.6 (9.2, NE)	0.7091 (0.4412, 1.1399) 0.1558	0.1540
No	98	29 (29.6)	69 (70.4)	NE (18.1, NE)	43	12 (27.9)	31 (72.1)	NE (7.2, NE)	0.7087 (0.3584, 1.4015) 0.3223	0.3359

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Age										0.2705
<65	289	74 (25.6)	215 (74.4)	NE (24.4, NE)	126	31 (24.6)	95 (75.4)	NE (9.2, NE)	0.6669 (0.4335, 1.0261) 0.0653	0.0649
>=65	82	29 (35.4)	53 (64.6)	16.5 (8.8, NE)	46	12 (26.1)	34 (73.9)	NE (5.5, NE)	0.8883 (0.4481, 1.7609) 0.7344	0.7368

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Age											
<75	357	100 (28.0)	257 (72.0)	NE (24.4, NE)	163	40 (24.5)	123 (75.5)	NE (9.2, NE)	0.7249 (0.4974, 1.0564) 0.0941	0.0945	0.6330
>=75	14	3 (21.4)	11 (78.6)	NE (5.1, NE)	9	3 (33.3)	6 (66.7)	NE (0.0, NE)	0.4582 (0.0908, 2.3130) 0.3448	0.3333	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Race										0.7219
White	175	50 (28.6)	125 (71.4)	24.4 (24.4, NE)	85	21 (24.7)	64 (75.3)	12.6 (9.2, NE)	0.7704 (0.4572, 1.2979) 0.3270	0.3257
Non-White	196	53 (27.0)	143 (73.0)	NE (18.1, NE)	86	22 (25.6)	64 (74.4)	NE (7.2, NE)	0.6539 (0.3925, 1.0895) 0.1029	0.1051

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Region										0.2133
Asia	147	38 (25.9)	109 (74.1)	NE (18.1, NE)	63	15 (23.8)	48 (76.2)	NE (NE, NE)	0.6027 (0.3258, 1.1149) 0.1067	0.1104
North America	58	24 (41.4)	34 (58.6)	11.1 (5.4, NE)	28	6 (21.4)	22 (78.6)	9.2 (4.4, NE)	1.3205 (0.5291, 3.2958) 0.5513	0.5530
Europe + Israel	166	41 (24.7)	125 (75.3)	24.4 (24.4, NE)	81	22 (27.2)	59 (72.8)	12.6 (7.2, NE)	0.6392 (0.3761, 1.0862) 0.0981	0.0949

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
ECOG PS										0.0737
0	199	37 (18.6)	162 (81.4)	NE (24.4, NE)	95	21 (22.1)	74 (77.9)	NE (12.6, NE)	0.4852 (0.2790, 0.8439) 0.0104	0.0092
1	172	66 (38.4)	106 (61.6)	13.1 (9.5, NE)	77	22 (28.6)	55 (71.4)	9.2 (9.2, NE)	0.9327 (0.5691, 1.5288) 0.7823	0.7860

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.8699
0	60	18 (30.0)	42 (70.0)	18.1 (8.7, NE)	31	10 (32.3)	21 (67.7)	NE (2.5, NE)	0.5039 (0.2258, 1.1243) 0.0942	0.0920
1	107	27 (25.2)	80 (74.8)	NE (16.5, NE)	48	10 (20.8)	38 (79.2)	NE (12.6, NE)	0.8415 (0.4033, 1.7558) 0.6456	0.6524
2	114	37 (32.5)	77 (67.5)	NE (11.8, NE)	50	15 (30.0)	35 (70.0)	NE (4.4, NE)	0.7345 (0.3972, 1.3580) 0.3251	0.3229

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	21 (23.3)	69 (76.7)	NE (24.4, NE)	43	8 (18.6)	35 (81.4)	NE (9.2, NE)	0.7581 (0.3248, 1.7695) 0.5219	0.5179	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Best Response to last prior cancer systemic therapy										0.2220
PD	173	46 (26.6)	127 (73.4)	24.4 (16.5, NE)	77	15 (19.5)	62 (80.5)	NE (7.2, NE)	0.8400 (0.4611, 1.5301)	0.5677
PR	48	12 (25.0)	36 (75.0)	NE (11.6, NE)	21	8 (38.1)	13 (61.9)	5.5 (1.7, NE)	0.3709 (0.1457, 0.9445)	0.0315
SD	82	22 (26.8)	60 (73.2)	NE (NE, NE)	54	12 (22.2)	42 (77.8)	NE (12.6, NE)	0.8508 (0.4141, 1.7479)	0.6586

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Reported history of CNS metastases										0.4378
Yes	37	12 (32.4)	25 (67.6)	24.4 (9.0, 24.4)	13	5 (38.5)	8 (61.5)	NE (0.8, NE)	0.3807 (0.1240, 1.1692) 0.0916	0.0808
No	334	91 (27.2)	243 (72.8)	NE (NE, NE)	159	38 (23.9)	121 (76.1)	NE (9.2, NE)	0.7490 (0.5086, 1.1032) 0.1435	0.1452

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.8097
Yes	24	9 (37.5)	15 (62.5)	24.4 (5.2, 24.4)	7	2 (28.6)	5 (71.4)	NE (0.1, NE)	0.7732 (0.1589, 3.7619)	0.7559
No	347	94 (27.1)	253 (72.9)	NE (NE, NE)	165	41 (24.8)	124 (75.2)	NE (9.2, NE)	0.7075 (0.4859, 1.0302)	0.0714

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Renal function at baseline										0.5324
Normal Function	201	51 (25.4)	150 (74.6)	24.4 (24.4, NE)	80	19 (23.8)	61 (76.3)	NE (9.2, NE)	0.6500 (0.3772, 1.1200) 0.1207	0.1189
Mild Impairment	123	36 (29.3)	87 (70.7)	NE (18.1, NE)	65	18 (27.7)	47 (72.3)	12.6 (4.7, NE)	0.6208 (0.3464, 1.1127) 0.1093	0.1093
Moderate Impairment	41	15 (36.6)	26 (63.4)	16.5 (6.2, NE)	23	6 (26.1)	17 (73.9)	NE (7.2, NE)	1.2033 (0.4650, 3.1138) 0.7029	0.7022

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hepatic function at baseline										0.0381
Normal Function	170	51 (30.0)	119 (70.0)	NE (NE, NE)	88	17 (19.3)	71 (80.7)	NE (NE, NE)	1.0127 (0.5794, 1.7701) 0.9647	0.9601
Mild Impairment	194	49 (25.3)	145 (74.7)	24.4 (18.1, NE)	82	26 (31.7)	56 (68.3)	12.6 (4.3, NE)	0.4825 (0.2945, 0.7903) 0.0038	0.0032

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline visceral disease										0.5773
Yes	331	94 (28.4)	237 (71.6)	24.4 (24.4, NE)	146	40 (27.4)	106 (72.6)	NE (9.2, NE)	0.6945 (0.4760, 1.0132) 0.0585	0.0581
No	40	9 (22.5)	31 (77.5)	NE (18.1, NE)	26	3 (11.5)	23 (88.5)	NE (NE, NE)	0.8351 (0.2023, 3.4478) 0.8033	0.8174

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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DE.T.4.2.2 - Serious Treatment-emergent adverse events - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (IXRS)										0.5676
Positive	329	89 (27.1)	240 (72.9)	NE (24.4, NE)	152	36 (23.7)	116 (76.3)	NE (9.2, NE)	0.7326 (0.4930, 1.0888)	0.1246
Negative	42	14 (33.3)	28 (66.7)	NE (7.3, NE)	20	7 (35.0)	13 (65.0)	4.7 (0.9, NE)	0.5723 (0.2180, 1.5023)	0.2537

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.2.2 - Serious Treatment-emergent adverse events - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (derived)										0.8354
Positive	331	90 (27.2)	241 (72.8)	NE (24.4, NE)	155	38 (24.5)	117 (75.5)	NE (9.2, NE)	0.7222 (0.4900, 1.0645) 0.1001	0.1009
Negative	40	13 (32.5)	27 (67.5)	NE (8.8, NE)	17	5 (29.4)	12 (70.6)	4.7 (2.5, NE)	0.5451 (0.1768, 1.6806) 0.2909	0.2851

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

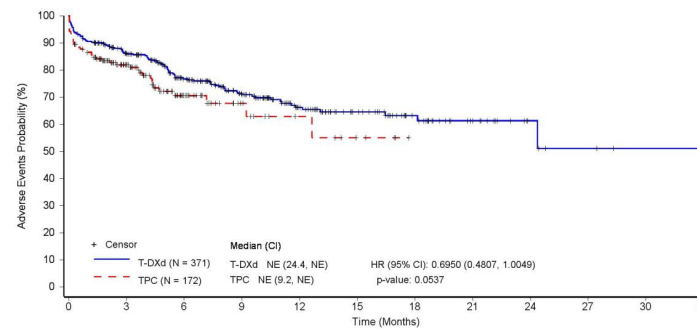
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Patients still at risk:

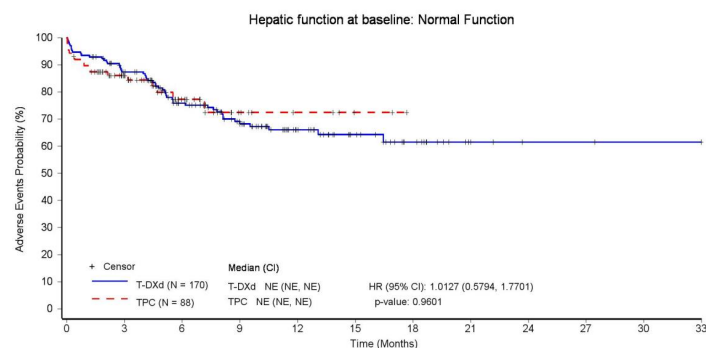
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	285	200	141	84	55	34	16	6	3	1	0
TPC (N = 172)	172	94	35	15	8	4	0	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

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 Run date: 21OCT2022 – 17:12; Program name: F4\_TEAE\_3\_SAS.sas; Output name: F4\_SAE\_3\_SAS.tf

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Patients still at risk:

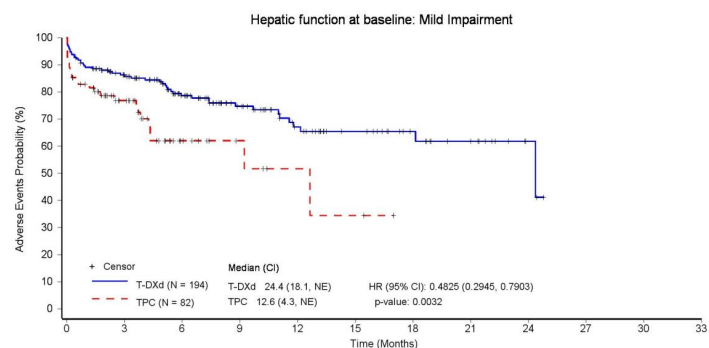
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 170)	170	139	102	76	43	27	15	4	2	2	1	0
TPC (N = 88)	88	88	54	22	9	5	2	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:12; Program name: F4\_TEAE\_4\_SAS.sas; Output name: F4\_SAE\_4\_SAS.tf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 194)	194	144	96	63	40	27	18	11	3	0	0	0
TPC (N = 82)	82	40	13	6	3	2	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:12; Program name: F4\_TEAE\_4\_SAS.sas; Output name: F4\_SAE\_4\_SAS.tf

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DE.T.4.3.1 - Severe Treatment-emergent adverse events (NCI CTCAE grade >= 3) - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	195 (52.6)	116 (67.4)	
Number of subjects censored, n (%)	176 (47.4)	56 (32.6)	
Median time to first event (months) [a]	7.6	0.9	
95% Confidence Interval	[5.2, 10.6]	[0.5, 1.7]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.4670
95% Confidence Interval			[0.3667, 0.5947]
p-value			<.0001
Stratified log-rank p-value [c]			<.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.3.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >= 3) - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
HER2 status											0.9953
HER2 IHC 1+	214	112 (52.3)	102 (47.7)	7.7 (5.0, 11.0)	100	67 (67.0)	33 (33.0)	0.7 (0.5, 2.0)	0.4752 (0.3483, 0.6485) <0.0001	<0.0001	
HER2 IHC 2+ /ISH Negative	157	83 (52.9)	74 (47.1)	7.2 (4.6, 13.3)	72	49 (68.1)	23 (31.9)	1.0 (0.5, 2.1)	0.4723 (0.3271, 0.6820) 0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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DE.T.4.3.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >= 3) - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.6989
1	220	101 (45.9)	119 (54.1)	10.5 (6.9, NE)	94	59 (62.8)	35 (37.2)	1.7 (0.5, 2.3)	0.4667 (0.3358, 0.6487)	<0.0001	
>=2	150	94 (62.7)	56 (37.3)	4.6 (3.1, 7.2)	78	57 (73.1)	21 (26.9)	0.5 (0.5, 1.0)	0.4884 (0.3460, 0.6892)	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.3.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >= 3) - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Prior CDK4/6											
Yes	233	116 (49.8)	117 (50.2)	9.0 (5.0, 13.1)	112	74 (66.1)	38 (33.9)	1.0 (0.5, 2.1)	0.4775 (0.3531, 0.6457) <0.0001	<0.0001	0.9626
No	98	56 (57.1)	42 (42.9)	6.4 (4.2, 12.5)	43	29 (67.4)	14 (32.6)	0.5 (0.3, 2.1)	0.4768 (0.3016, 0.7540) 0.0015	0.0014	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.3.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >= 3) - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											
<65	289	143 (49.5)	146 (50.5)	8.4 (6.3, 13.1)	126	83 (65.9)	43 (34.1)	0.9 (0.5, 1.9)	0.4391 (0.3316, 0.5816)	<0.0001	0.2111
>=65	82	52 (63.4)	30 (36.6)	4.0 (2.1, 7.6)	46	33 (71.7)	13 (28.3)	0.6 (0.3, 2.8)	0.6157 (0.3955, 0.9584)	0.0320	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											
<75	357	189 (52.9)	168 (47.1)	7.6 (5.2, 10.6)	163	109 (66.9)	54 (33.1)	0.8 (0.5, 1.7)	0.4740 (0.3714, 0.6049)	<0.0001	0.8432
>=75	14	6 (42.9)	8 (57.1)	NE (0.3, NE)	9	7 (77.8)	2 (22.2)	1.4 (0.2, 4.7)	0.4346 (0.1447, 1.3058)	0.1213	0.1376

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.3.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >= 3) - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Race											0.5089
White	175	83 (47.4)	92 (52.6)	9.7 (5.5, NE)	85	53 (62.4)	32 (37.6)	2.1 (0.9, 4.3)	0.4978 (0.3485, 0.7111) 0.0001	<0.0001	
Non-White	196	112 (57.1)	84 (42.9)	5.5 (3.7, 8.4)	86	63 (73.3)	23 (26.7)	0.5 (0.3, 0.5)	0.4215 (0.3062, 0.5801) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.3.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >= 3) - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Region											0.2779
Asia	147	87 (59.2)	60 (40.8)	4.9 (2.8, 8.2)	63	48 (76.2)	15 (23.8)	0.3 (0.3, 0.5)	0.3547 (0.2453, 0.5128) <0.0001	<0.0001	
North America	58	29 (50.0)	29 (50.0)	8.4 (5.2, NE)	28	20 (71.4)	8 (28.6)	1.0 (0.5, 4.4)	0.4300 (0.2351, 0.7863) 0.0061	0.0051	
Europe + Israel	166	79 (47.6)	87 (52.4)	10.6 (5.5, NE)	81	48 (59.3)	33 (40.7)	2.1 (0.9, 4.3)	0.5607 (0.3879, 0.8104) 0.0021	0.0018	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
ECOG PS											
0	199	93 (46.7)	106 (53.3)	12.0 (7.1, NE)	95	58 (61.1)	37 (38.9)	1.9 (0.5, 2.8)	0.4593 (0.3277, 0.6438)	<0.0001	0.7553
1	172	102 (59.3)	70 (40.7)	4.9 (2.9, 7.8)	77	58 (75.3)	19 (24.7)	0.5 (0.5, 1.0)	0.4745 (0.3390, 0.6640)	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1426
0	60	30 (50.0)	30 (50.0)	7.8 (4.2, NE)	31	24 (77.4)	7 (22.6)	0.3 (0.2, 0.8)	0.2816 (0.1549, 0.5121) <0.0001	<0.0001	
1	107	57 (53.3)	50 (46.7)	7.7 (4.2, 13.3)	48	33 (68.8)	15 (31.3)	1.9 (0.5, 3.2)	0.5006 (0.3232, 0.7753) 0.0019	0.0017	
2	114	65 (57.0)	49 (43.0)	4.9 (2.1, 10.5)	50	31 (62.0)	19 (38.0)	0.7 (0.5, 4.4)	0.6869 (0.4447, 1.0608) 0.0903	0.0948	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	43 (47.8)	47 (52.2)	11.0 (5.3, 24.4)	43	28 (65.1)	15 (34.9)	1.0 (0.5, 2.3)	0.3785 (0.2278, 0.6289) 0.0002	0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.1322
PD	173	90 (52.0)	83 (48.0)	7.7 (4.0, 13.1)	77	48 (62.3)	29 (37.7)	0.7 (0.5, 2.8)	0.5077 (0.3529, 0.7303) 0.0003	0.0002	
PR	48	26 (54.2)	22 (45.8)	7.6 (3.0, 19.4)	21	17 (81.0)	4 (19.0)	0.3 (0.2, 0.5)	0.2738 (0.1434, 0.5228) 0.0001	<0.0001	
SD	82	46 (56.1)	36 (43.9)	5.0 (2.8, 11.0)	54	36 (66.7)	18 (33.3)	1.0 (0.5, 2.3)	0.6116 (0.3921, 0.9539) 0.0302	0.0287	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Reported history of CNS metastases											
Yes	37	18 (48.6)	19 (51.4)	24.4 (0.8, 24.4)	13	9 (69.2)	4 (30.8)	0.5 (0.3, NE)	0.4702 (0.2075, 1.0652) 0.0705	0.0709	0.6845
No	334	177 (53.0)	157 (47.0)	7.6 (5.2, 10.5)	159	107 (67.3)	52 (32.7)	0.9 (0.5, 1.9)	0.4744 (0.3703, 0.6077) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Baseline CNS metastases											0.2934
Yes	24	16 (66.7)	8 (33.3)	0.9 (0.3, 24.4)	7	4 (57.1)	3 (42.9)	0.8 (0.1, NE)	0.9503 (0.3123, 2.8915)	0.9062	
No	347	179 (51.6)	168 (48.4)	7.8 (5.4, 11.0)	165	112 (67.9)	53 (32.1)	0.9 (0.5, 1.7)	0.4540 (0.3558, 0.5794)	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Renal function at baseline											0.3863
Normal Function	201	101 (50.2)	100 (49.8)	8.1 (5.3, 12.9)	80	53 (66.3)	27 (33.8)	1.0 (0.5, 2.0)	0.4334 (0.3070, 0.6120)	<0.0001	
Mild Impairment	123	63 (51.2)	60 (48.8)	7.7 (4.2, 15.2)	65	45 (69.2)	20 (30.8)	0.5 (0.5, 1.4)	0.4423 (0.2979, 0.6569)	<0.0001	
Moderate Impairment	41	26 (63.4)	15 (36.6)	4.5 (0.5, 10.6)	23	16 (69.6)	7 (30.4)	1.0 (0.5, 3.2)	0.7194 (0.3811, 1.3580)	0.3240	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hepatic function at baseline											0.6087
Normal Function	170	86 (50.6)	84 (49.4)	8.1 (6.4, 19.4)	88	58 (65.9)	30 (34.1)	0.7 (0.5, 2.0)	0.4301 (0.3048, 0.6069)	<0.0001	
Mild Impairment	194	104 (53.6)	90 (46.4)	6.2 (4.0, 11.0)	82	57 (69.5)	25 (30.5)	1.0 (0.5, 2.1)	0.4931 (0.3533, 0.6881)	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Baseline visceral disease											0.2599
Yes	331	175 (52.9)	156 (47.1)	7.0 (5.0, 10.5)	146	98 (67.1)	48 (32.9)	1.0 (0.5, 2.0)	0.5011 (0.3887, 0.6460)	<0.0001	
No	40	20 (50.0)	20 (50.0)	12.5 (5.2, NE)	26	18 (69.2)	8 (30.8)	0.5 (0.3, 1.9)	0.3171 (0.1578, 0.6375)	0.0007	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (IXRS)											
Positive	329	170 (51.7)	159 (48.3)	7.8 (5.4, 11.0)	152	100 (65.8)	52 (34.2)	0.9 (0.5, 2.0)	0.4786 (0.3711, 0.6171)	<0.0001	0.9159
Negative	42	25 (59.5)	17 (40.5)	4.0 (1.0, 19.4)	20	16 (80.0)	4 (20.0)	0.7 (0.2, 1.9)	0.4353 (0.2229, 0.8503)	0.0110	0.0149

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Run date: 13SEP2022 – 17:10; Program name: T4\_TEAE\_2\_SAS.sas; Output name: T4\_AESEV\_2\_SAS.rtf

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DE.T.4.3.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >= 3) - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (derived)											0.8354
Positive	331	173 (52.3)	158 (47.7)	7.8 (5.3, 11.0)	155	103 (66.5)	52 (33.5)	0.9 (0.5, 1.9)	0.4775 (0.3713, 0.6141)	<0.0001	
Negative	40	22 (55.0)	18 (45.0)	4.2 (1.6, NE)	17	13 (76.5)	4 (23.5)	0.7 (0.2, 2.4)	0.4264 (0.2070, 0.8782)	0.0164	

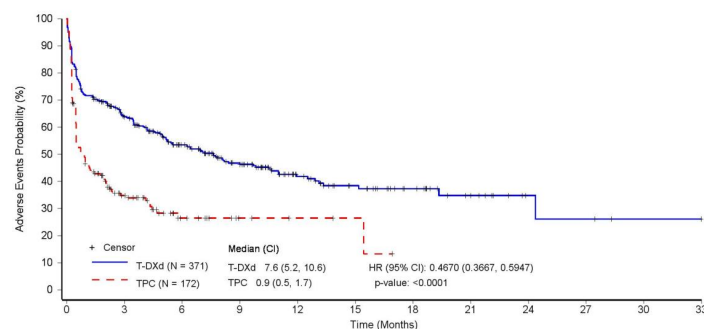
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.F.4.3.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade >= 3) - Kaplan-Meier plot - Destiny Breast 04 - DCO  
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Patients still at risk:

T-DXd (N = 371)	371	211	144	96	53	35	22	11	4	3	1	0
TPC (N = 172)	172	41	13	5	3	2	0	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:12; Program name: F4\_TEAE\_3\_SAS.sas; Output name: F4\_AESEV\_3\_SAS.rf

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DE.F.4.3.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >= 3) - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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No significant interaction has been found

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Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
Run date: 21OCT2022 – 17:12; Program name: F4\_TEAE\_4\_SAS.sas; Output name: F4\_AESEV\_4\_SAS.rtf

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DE.T.4.4.1 - Non-severe Treatment-emergent adverse events (NCI CTCAE grade < 3) - Descriptive summary - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

	T-DXd (N=371)	TPC (N=172)
Number of subjects with events, n (%)	367(98.9)	169(98.3)

N: number of subjects in analysis set, n: number of subjects with events; %: proportion of number of subjects in analysis set

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.5.1 - Treatment-emergent adverse events associated with discontinuation of study treatment - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	60 (16.2)	14 (8.1)	
Number of subjects censored, n (%)	311 (83.8)	158 (91.9)	
Median time to first event (months) [a]	NE	NE	
95% Confidence Interval	[24.4, NE]	[16.2, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			1.1171
95% Confidence Interval			[0.6125, 2.0375]
p-value			0.7180
Stratified log-rank p-value [c]			0.7180

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.5.2 - Treatment-emergent adverse events associated with discontinuation of study treatment - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
HER2 status											0.8835
HER2 IHC 1+	214	36 (16.8)	178 (83.2)	NE (NE, NE)	100	8 (8.0)	92 (92.0)	NE (NE, NE)	1.1638 (0.5319, 2.5466)	0.7036	
HER2 IHC 2+/ISH Negative	157	24 (15.3)	133 (84.7)	NE (24.4, NE)	72	6 (8.3)	66 (91.7)	NE (16.2, NE)	1.0645 (0.4270, 2.6537)	0.8931	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.5.2 - Treatment-emergent adverse events associated with discontinuation of study treatment - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.6691
1	220	36 (16.4)	184 (83.6)	NE (24.4, NE)	94	9 (9.6)	85 (90.4)	NE (16.2, NE)	1.0327 (0.4896, 2.1784)	0.9327	
>=2	150	24 (16.0)	126 (84.0)	NE (NE, NE)	78	5 (6.4)	73 (93.6)	NE (NE, NE)	1.2395 (0.4642, 3.3100)	0.6684	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.5.2 - Treatment-emergent adverse events associated with discontinuation of study treatment - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Prior CDK4/6											
Yes	233	37 (15.9)	196 (84.1)	24.4 (24.4, NE)	112	9 (8.0)	103 (92.0)	NE (NE, NE)	1.1095 (0.5262, 2.3396) 0.7848	0.7839	0.7532
No	98	14 (14.3)	84 (85.7)	NE (NE, NE)	43	4 (9.3)	39 (90.7)	NE (16.2, NE)	0.8944 (0.2873, 2.7849) 0.8473	0.8472	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											
<65	289	40 (13.8)	249 (86.2)	NE (24.4, NE)	126	12 (9.5)	114 (90.5)	NE (16.2, NE)	0.7305 (0.3752, 1.4226)	0.3545	0.0245
>=65	82	20 (24.4)	62 (75.6)	NE (15.2, NE)	46	2 (4.3)	44 (95.7)	NE (NE, NE)	4.0172 (0.9307, 17.3404)	0.0441	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											0.3189
<75	357	55 (15.4)	302 (84.6)	NE (24.4, NE)	163	13 (8.0)	150 (92.0)	NE (16.2, NE)	1.0443 (0.5621, 1.9399)	0.8895	
>=75	14	5 (35.7)	9 (64.3)	13.8 (3.3, NE)	9	1 (11.1)	8 (88.9)	NE (0.6, NE)	3.1656 (0.3686, 27.1855)	0.2675	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Race											0.9985
White	175	30 (17.1)	145 (82.9)	24.4 (24.4, NE)	85	7 (8.2)	78 (91.8)	NE (NE, NE)	1.2164 (0.5241, 2.8232)	0.6466	
Non-White	196	30 (15.3)	166 (84.7)	NE (NE, NE)	86	7 (8.1)	79 (91.9)	NE (16.2, NE)	1.0327 (0.4468, 2.3868)	0.9407	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Region											0.7093
Asia	147	26 (17.7)	121 (82.3)	NE (NE, NE)	63	4 (6.3)	59 (93.7)	16.2 (16.2, NE)	1.5645 (0.5383, 4.5466) 0.4110	0.4081	
North America	58	8 (13.8)	50 (86.2)	NE (NE, NE)	28	2 (7.1)	26 (92.9)	NE (NE, NE)	1.1707 (0.2430, 5.6407) 0.8443	0.8441	
Europe + Israel	166	26 (15.7)	140 (84.3)	24.4 (20.4, NE)	81	8 (9.9)	73 (90.1)	NE (NE, NE)	0.8875 (0.3918, 2.0105) 0.7749	0.7765	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
ECOG PS											
0	199	30 (15.1)	169 (84.9)	NE (24.4, NE)	95	8 (8.4)	87 (91.6)	NE (16.2, NE)	0.8955 (0.4031, 1.9896)	0.7857	0.5560
1	172	30 (17.4)	142 (82.6)	NE (20.4, NE)	77	6 (7.8)	71 (92.2)	NE (NE, NE)	1.4466 (0.5925, 3.5317)	0.4156	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.7599
0	60	16 (26.7)	44 (73.3)	18.1 (12.5, NE)	31	4 (12.9)	27 (87.1)	16.2 (NE, NE)	0.9412 (0.3053, 2.9020)	0.9160	0.9160
1	107	17 (15.9)	90 (84.1)	NE (20.4, NE)	48	3 (6.3)	45 (93.8)	NE (NE, NE)	1.8664 (0.5383, 6.4712)	0.3178	0.3253
2	114	16 (14.0)	98 (86.0)	NE (NE, NE)	50	4 (8.0)	46 (92.0)	NE (NE, NE)	1.0163 (0.3300, 3.1303)	0.9756	0.9775

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	11 (12.2)	79 (87.8)	NE (24.4, NE)	43	3 (7.0)	40 (93.0)	NE (NE, NE)	0.7273 (0.1932, 2.7373) 0.6377	0.6356	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.7334
PD	173	30 (17.3)	143 (82.7)	NE (24.4, NE)	77	6 (7.8)	71 (92.2)	NE (NE, NE)	1.2857 (0.5260, 3.1429)	0.5816	0.5811
PR	48	10 (20.8)	38 (79.2)	NE (12.6, NE)	21	2 (9.5)	19 (90.5)	NE (NE, NE)	0.8209 (0.1639, 4.1107)	0.8102	0.8100
SD	82	9 (11.0)	73 (89.0)	NE (NE, NE)	54	5 (9.3)	49 (90.7)	NE (16.2, NE)	0.8934 (0.2959, 2.6971)	0.8415	0.8414

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Reported history of CNS metastases											0.3280
Yes	37	3 (8.1)	34 (91.9)	24.4 (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9977	0.5315	
No	334	57 (17.1)	277 (82.9)	NE (NE, NE)	159	14 (8.8)	145 (91.2)	NE (16.2, NE)	1.1117 (0.6120, 2.0194) 0.7280	0.7278	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Baseline CNS metastases											0.2980
Yes	24	3 (12.5)	21 (87.5)	24.4 (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9971	0.4137	
No	347	57 (16.4)	290 (83.6)	NE (NE, NE)	165	14 (8.5)	151 (91.5)	NE (16.2, NE)	1.0723 (0.5900, 1.9489) 0.8188	0.8186	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Renal function at baseline											0.1227
Normal Function	201	26 (12.9)	175 (87.1)	NE (24.4, NE)	80	7 (8.8)	73 (91.3)	16.2 (16.2, NE)	0.7948 (0.3360, 1.8800) 0.6011	0.5996	
Mild Impairment	123	20 (16.3)	103 (83.7)	NE (20.4, NE)	65	5 (7.7)	60 (92.3)	NE (NE, NE)	1.0749 (0.3907, 2.9574) 0.8888	0.8901	
Moderate Impairment	41	12 (29.3)	29 (70.7)	NE (11.0, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	5.5351 (0.7189, 42.6141) 0.1004	0.0643	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hepatic function at baseline											0.1849
Normal Function	170	23 (13.5)	147 (86.5)	NE (NE, NE)	88	9 (10.2)	79 (89.8)	NE (16.2, NE)	0.7837 (0.3574, 1.7184)	0.5416	
Mild Impairment	194	36 (18.6)	158 (81.4)	24.4 (20.4, NE)	82	5 (6.1)	77 (93.9)	NE (NE, NE)	1.5734 (0.6058, 4.0864)	0.3487	
									0.3520		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Baseline visceral disease											0.8145
Yes	331	53 (16.0)	278 (84.0)	NE (24.4, NE)	146	12 (8.2)	134 (91.8)	NE (16.2, NE)	1.1582 (0.6121, 2.1914)	0.6518	
No	40	7 (17.5)	33 (82.5)	NE (18.1, NE)	26	2 (7.7)	24 (92.3)	NE (NE, NE)	0.8293 (0.1531, 4.4920)	0.8279	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (IXRS)											0.8743
Positive	329	50 (15.2)	279 (84.8)	NE (24.4, NE)	152	12 (7.9)	140 (92.1)	NE (16.2, NE)	1.0802 (0.5673, 2.0567) 0.8144	0.8143	
Negative	42	10 (23.8)	32 (76.2)	NE (8.3, NE)	20	2 (10.0)	18 (90.0)	NE (NE, NE)	1.2139 (0.2472, 5.9598) 0.8113	0.8110	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (derived)											0.5236
Positive	331	51 (15.4)	280 (84.6)	NE (24.4, NE)	155	13 (8.4)	142 (91.6)	NE (16.2, NE)	1.0428 (0.5593, 1.9439)	0.8952	0.8936
Negative	40	9 (22.5)	31 (77.5)	NE (8.3, NE)	17	1 (5.9)	16 (94.1)	NE (2.9, NE)	1.6556 (0.1941, 14.1204)	0.6448	0.6414

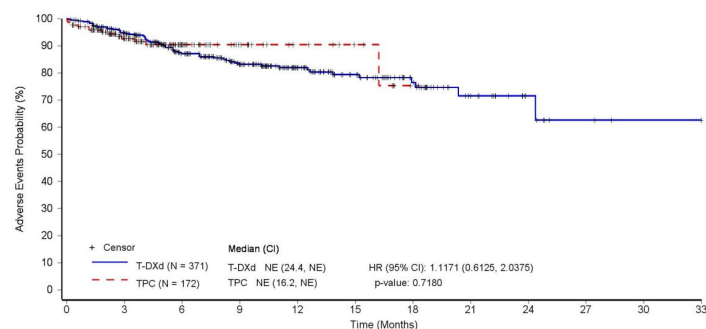
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:10; Program name: T4\_TEAE\_2\_SAS.sas; Output name: T4\_AEDISC\_2\_SAS.rtf



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Patients still at risk:

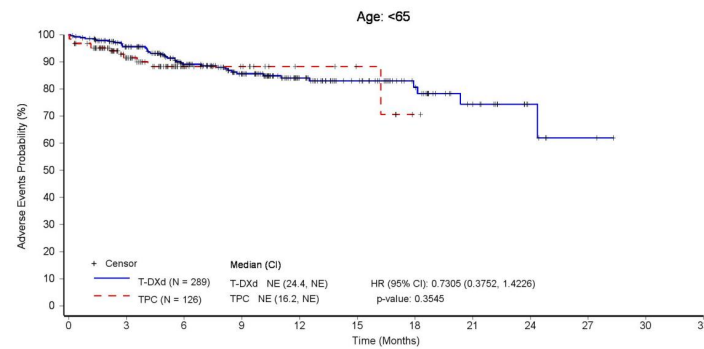
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	309	230	169	109	73	43	19	8	3	1	0
TPC (N = 172)	172	100	42	20	11	7	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:12; Program name: F4\_TEAE\_3\_SAS.sas; Output name: F4\_AEDISC\_3\_SAS.rf

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Patients still at risk:

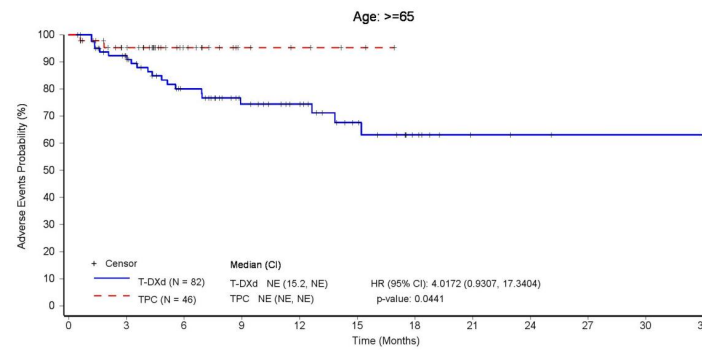
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 289)	289	244	183	136	83	57	35	16	6	2	0	0
TPC (N = 126)	126	67	27	14	7	5	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:12; Program name: F4\_TEAE\_4\_SAS.sas; Output name: F4\_AEDISC\_4\_SAS.rf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 82)	82	65	47	33	26	16	8	3	2	1	1	0
TPC (N = 46)	46	33	15	6	4	2	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:12; Program name: F4\_TEAE\_4\_SAS.sas; Output name: F4\_AEDISC\_4\_SAS.rf

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DE.T.4.6.1 - Treatment-emergent adverse events - NCI CTCAE grade 1 - Descriptive summary - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

	T-DXd (N=371)	TPC (N=172)
Number of subjects with events, n (%)	355(95.7)	163(94.8)

N: number of subjects in analysis set, n: number of subjects with events; %: proportion of number of subjects in analysis set

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:12; Program name: T4\_AENONSEV\_1\_SAS.sas; Output name: T4\_AESEVGRADE\_1\_SAS.rtf

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DE.T.4.6.2 - Treatment-emergent adverse events - NCI CTCAE grade 2 - Descriptive summary - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

	T-DXd (N=371)	TPC (N=172)
Number of subjects with events, n (%)	323(87.1)	138(80.2)

N: number of subjects in analysis set, n: number of subjects with events; %: proportion of number of subjects in analysis set

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:12; Program name: T4\_AENONSEV\_1\_SAS.sas; Output name: T4\_AESEVGRADE\_2\_SAS.rtf

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DE.T.4.6.3 - Treatment-emergent adverse events - NCI CTCAE grade 3 - Descriptive summary - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

	T-DXd (N=371)	TPC (N=172)
Number of subjects with events, n (%)	191(51.5)	110(64.0)

N: number of subjects in analysis set, n: number of subjects with events; %: proportion of number of subjects in analysis set

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:12; Program name: T4\_AENONSEV\_1\_SAS.sas; Output name: T4\_AESEVGRADE\_3\_SAS.rtf

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DE.T.4.6.4 - Treatment-emergent adverse events - NCI CTCAE grade 4 - Descriptive summary - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

	T-DXd (N=371)	TPC (N=172)
Number of subjects with events, n (%)	39(10.5)	37(21.5)

N: number of subjects in analysis set, n: number of subjects with events; %: proportion of number of subjects in analysis set

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:13; Program name: T4\_AENONSEV\_1\_SAS.sas; Output name: T4\_AESEVGRADE\_4\_SAS.rtf

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DE.T.4.6.5 - Treatment-emergent adverse events - NCI CTCAE grade 5 - Descriptive summary - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

	T-DXd (N=371)	TPC (N=172)
Number of subjects with events, n (%)	14(3.8)	5(2.9)

N: number of subjects in analysis set, n: number of subjects with events; %: proportion of number of subjects in analysis set

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:13; Program name: T4\_AENONSEV\_1\_SAS.sas; Output name: T4\_AESEVGRADE\_5\_SAS.rtf



**Anhang 4-G 4.2: Unerwünschte Ereignisse von besonderem Interesse**

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DE.T.4.14.1 - Adverse events of special interest - Adjudicated Interstitial lung disease/pneumonitis (ILD) - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	46 (12.4)	1 (0.6)	
Number of subjects censored, n (%)	325 (87.6)	171 (99.4)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			13.5879 [1.8593, 99.2998] 0.0101
Stratified log-rank p-value [c]			0.0008

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:09; Program name: T4\_TEAE\_1\_SAS.sas; Output name: T4\_AESILDAC\_1\_SAS.rtf

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DE.T.4.14.2 - Adverse events of special interest - Adjudicated Interstitial lung disease/pneumonitis (ILD) - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO  
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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
HER2 status											0.2031
HER2 IHC 1+	214	26 (12.1)	188 (87.9)	NE (NE, NE)	100	0	100 (100)	NE (NE, NE)	NE (NE, NE) 0.9907	0.0084	
HER2 IHC 2+/ISH Negative	157	20 (12.7)	137 (87.3)	NE (23.3, NE)	72	1 (1.4)	71 (98.6)	NE (NE, NE)	5.4015 (0.7170, 40.6943) 0.1016	0.0667	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:09; Program name: T4\_TEAE\_2\_SAS.sas; Output name: T4\_AESILDAC\_2\_SAS.rtf

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.1939
1	220	27 (12.3)	193 (87.7)	NE (23.3, NE)	94	0	94 (100)	NE (NE, NE)	NE (NE, NE) 0.9905	0.0074	
>=2	150	19 (12.7)	131 (87.3)	NE (NE, NE)	78	1 (1.3)	77 (98.7)	NE (NE, NE)	5.1867 (0.6853, 39.2528) 0.1109	0.0760	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Prior CDK4/6											
Yes	233	29 (12.4)	204 (87.6)	NE (NE, NE)	112	1 (0.9)	111 (99.1)	NE (NE, NE)	8.1653 (1.1050, 60.3343) 0.0396	0.0142	0.4176
No	98	11 (11.2)	87 (88.8)	NE (23.3, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9940	0.0892	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:09; Program name: T4\_TEAE\_2\_SAS.sas; Output name: T4\_AESILDAC\_2\_SAS.rtf

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											
<65	289	31 (10.7)	258 (89.3)	NE (NE, NE)	126	1 (0.8)	125 (99.2)	NE (NE, NE)	7.1730 (0.9718, 52.9446) 0.0534	0.0241	0.2735
>=65	82	15 (18.3)	67 (81.7)	NE (15.2, NE)	46	0	46 (100)	NE (NE, NE)	NE (NE, NE) 0.9919	0.0153	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											0.5843
<75	357	43 (12.0)	314 (88.0)	NE (NE, NE)	163	1 (0.6)	162 (99.4)	NE (NE, NE)	11.1145 (1.5217, 81.1815) 0.0176	0.0029	
>=75	14	3 (21.4)	11 (78.6)	NE (5.5, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9973	0.1415	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:09; Program name: T4\_TEAE\_2\_SAS.sas; Output name: T4\_AESILDAC\_2\_SAS.rtf

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Race											0.1990
White	175	20 (11.4)	155 (88.6)	NE (NE, NE)	85	1 (1.2)	84 (98.8)	NE (NE, NE)	6.0585 (0.8062, 45.5301) 0.0800	0.0462	
Non-White	196	26 (13.3)	170 (86.7)	NE (23.3, NE)	86	0	86 (100)	NE (NE, NE)	NE (NE, NE) 0.9910	0.0123	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Region											0.3874
Asia	147	22 (15.0)	125 (85.0)	NE (23.3, NE)	63	0	63 (100)	NE (NE, NE)	NE (NE, NE) 0.9918	0.0225	
North America	58	8 (13.8)	50 (86.2)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9948	0.1375	
Europe + Israel	166	16 (9.6)	150 (90.4)	NE (NE, NE)	81	1 (1.2)	80 (98.8)	NE (NE, NE)	4.9650 (0.6514, 37.8441) 0.1220	0.0865	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
ECOG PS											
0	199	24 (12.1)	175 (87.9)	NE (23.3, NE)	95	1 (1.1)	94 (98.9)	NE (NE, NE)	6.3031 (0.8430, 47.1294) 0.0729	0.0402	0.2498
1	172	22 (12.8)	150 (87.2)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE) 0.9913	0.0133	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)									0.4369
0	60	10 (16.7)	50 (83.3)	NE (12.5, NE)	31	0	31 (100)	NE (NE, NE) 0.9943	0.1070
1	107	11 (10.3)	96 (89.7)	NE (NE, NE)	48	0	48 (100)	NE (NE, NE) 0.9932	0.0441
2	114	14 (12.3)	100 (87.7)	NE (23.3, NE)	50	1 (2.0)	49 (98.0)	NE (NE, NE) 2.8392 (0.3602, 22.3790) 0.3219	0.3007

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	11 (12.2)	79 (87.8)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9943	0.1130	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.3679
PD	173	20 (11.6)	153 (88.4)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE) 0.9919	0.0219	
PR	48	7 (14.6)	41 (85.4)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	NE (NE, NE) 0.9942	0.3264	
SD	82	9 (11.0)	73 (89.0)	23.3 (23.3, NE)	54	1 (1.9)	53 (98.1)	NE (NE, NE)	4.5694 (0.5674, 36.7985) 0.1534	0.1174	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Reported history of CNS metastases											
Yes	37	3 (8.1)	34 (91.9)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (2.0, NE)	0.5125 (0.0494, 5.3204)	0.5691	0.0139
No	334	43 (12.9)	291 (87.1)	NE (23.3, NE)	159	0	159 (100)	NE (NE, NE)	NE (NE, NE)	0.0005	0.9879

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Baseline CNS metastases											0.8542
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.5637	
No	347	45 (13.0)	302 (87.0)	NE (23.3, NE)	165	1 (0.6)	164 (99.4)	NE (NE, NE)	12.1702 (1.6685, 88.7689) 0.0137	0.0016	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Renal function at baseline											0.3520
Normal Function	201	21 (10.4)	180 (89.6)	NE (23.3, NE)	80	1 (1.3)	79 (98.8)	NE (NE, NE)	4.6115 (0.6103, 34.8457) 0.1385	0.1039	
Mild Impairment	123	15 (12.2)	108 (87.8)	NE (NE, NE)	65	0	65 (100)	NE (NE, NE)	NE (NE, NE) 0.9929	0.0425	
Moderate Impairment	41	9 (22.0)	32 (78.0)	NE (15.2, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9934	0.0422	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hepatic function at baseline											0.2362
Normal Function	170	20 (11.8)	150 (88.2)	NE (NE, NE)	88	0	88 (100)	NE (NE, NE)	NE (NE, NE) 0.9912	0.0111	
Mild Impairment	194	26 (13.4)	168 (86.6)	NE (23.3, NE)	82	1 (1.2)	81 (98.8)	NE (NE, NE)	5.7193 (0.7661, 42.6961) 0.0891	0.0550	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Baseline visceral disease											
Yes	331	42 (12.7)	289 (87.3)	NE (23.3, NE)	146	1 (0.7)	145 (99.3)	NE (NE, NE)	11.2270 (1.5379, 81.9606) 0.0171	0.0027	0.6608
No	40	4 (10.0)	36 (90.0)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9967	0.3156	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Run date: 13SEP2022 – 17:09; Program name: T4\_TEAE\_2\_SAS.sas; Output name: T4\_AESILDAC\_2\_SAS.rtf

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (IXRS)											0.5678
Positive	329	39 (11.9)	290 (88.1)	NE (NE, NE)	152	1 (0.7)	151 (99.3)	NE (NE, NE)	10.5925 (1.4474, 77.5180) 0.0201	0.0038	
Negative	42	7 (16.7)	35 (83.3)	NE (12.5, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) 0.9957	0.1988	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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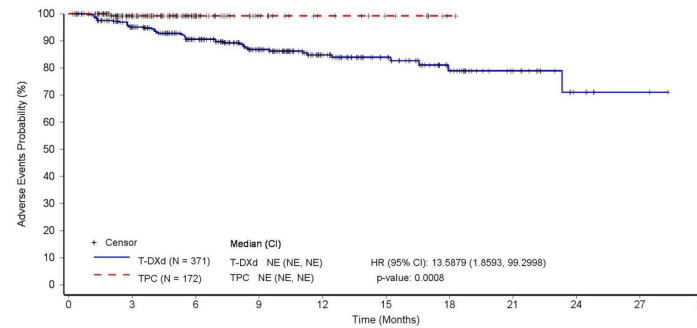
Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (derived)											0.6017
Positive	331	39 (11.8)	292 (88.2)	NE (NE, NE)	155	1 (0.6)	154 (99.4)	NE (NE, NE)	11.0438 (1.5095, 80.7992) 0.0180	0.0030	
Negative	40	7 (17.5)	33 (82.5)	NE (11.1, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) 0.9947	0.3295	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:09; Program name: T4\_TEAE\_2\_SAS.sas; Output name: T4\_AESILDAC\_2\_SAS.rtf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 371)	371	304	229	163	102	68	37	18	6	2	0
TPC (N = 172)	172	106	44	20	11	7	1	0	0	0	0

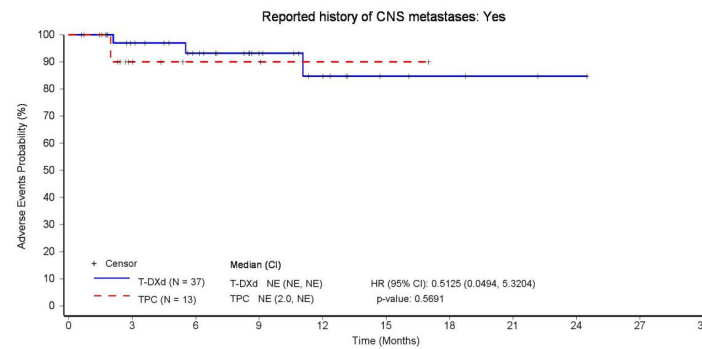
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:12; Program name: F4\_TEAE\_3\_SAS.sas; Output name: F4\_AESIILDAC\_3\_SAS.rtf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 37)	37	30	23	15	9	4	3	2	1	0	0
TPC (N = 13)	13	5	2	2	1	1	0	0	0	0	0

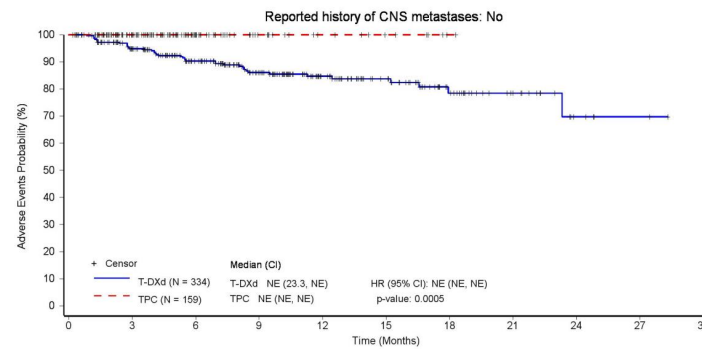
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:12; Program name: F4\_TEAE\_4\_SAS.sas; Output name: F4\_AESIILDAC\_4\_SAS.tf

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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 334)	334	274	206	148	93	64	34	16	5	2	0
TPC (N = 159)	159	101	42	18	10	6	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:12; Program name: F4\_TEAE\_4\_SAS.sas; Output name: F4\_AESIILDAC\_4\_SAS.rtf

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DE.T.4.15.1 - Adverse events of special interest - Drug-related adjudicated Interstitial lung disease/pneumonitis (ILD) - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	45 (12.1)	1 (0.6)	
Number of subjects censored, n (%)	326 (87.9)	171 (99.4)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			12.7480 [1.7448, 93.1395] 0.0121
Stratified log-rank p-value [c]			0.0012

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:09; Program name: T4\_TEAE\_1\_SAS.sas; Output name: T4\_AESILDDRAC\_1\_SAS.rtf



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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
HER2 status											0.2092
HER2 IHC 1+	214	25 (11.7)	189 (88.3)	NE (NE, NE)	100	0	100 (100)	NE (NE, NE)	NE (NE, NE) 0.9909	0.0103	
HER2 IHC 2+/ISH Negative	157	20 (12.7)	137 (87.3)	NE (23.3, NE)	72	1 (1.4)	71 (98.6)	NE (NE, NE)	5.4015 (0.7170, 40.6943) 0.1016	0.0667	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.1999
1	220	26 (11.8)	194 (88.2)	NE (23.3, NE)	94	0	94 (100)	NE (NE, NE)	NE (NE, NE) 0.9907	0.0090	
>=2	150	19 (12.7)	131 (87.3)	NE (NE, NE)	78	1 (1.3)	77 (98.7)	NE (NE, NE)	5.1867 (0.6853, 39.2528) 0.1109	0.0760	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Prior CDK4/6											
Yes	233	29 (12.4)	204 (87.6)	NE (NE, NE)	112	1 (0.9)	111 (99.1)	NE (NE, NE)	8.1653 (1.1050, 60.3343) 0.0396	0.0142	0.4176
No	98	11 (11.2)	87 (88.8)	NE (23.3, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9940	0.0892	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											
<65	289	30 (10.4)	259 (89.6)	NE (NE, NE)	126	1 (0.8)	125 (99.2)	NE (NE, NE)	6.8528 (0.9268, 50.6697) 0.0594	0.0289	0.2674
>=65	82	15 (18.3)	67 (81.7)	NE (15.2, NE)	46	0	46 (100)	NE (NE, NE)	NE (NE, NE) 0.9919	0.0153	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											
<75	357	42 (11.8)	315 (88.2)	NE (NE, NE)	163	1 (0.6)	162 (99.4)	NE (NE, NE)	10.7582 (1.4716, 78.6457) 0.0193	0.0035	0.5792
>=75	14	3 (21.4)	11 (78.6)	NE (5.5, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9973	0.1415	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Race											0.2052
White	175	20 (11.4)	155 (88.6)	NE (NE, NE)	85	1 (1.2)	84 (98.8)	NE (NE, NE)	6.0585 (0.8062, 45.5301) 0.0800	0.0462	
Non-White	196	25 (12.8)	171 (87.2)	NE (23.3, NE)	86	0	86 (100)	NE (NE, NE)	NE (NE, NE) 0.9913	0.0150	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Region											0.3956
Asia	147	21 (14.3)	126 (85.7)	NE (23.3, NE)	63	0	63 (100)	NE (NE, NE)	NE (NE, NE) 0.9921	0.0272	
North America	58	8 (13.8)	50 (86.2)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9948	0.1375	
Europe + Israel	166	16 (9.6)	150 (90.4)	NE (NE, NE)	81	1 (1.2)	80 (98.8)	NE (NE, NE)	4.9650 (0.6514, 37.8441) 0.1220	0.0865	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
ECOG PS											
0	199	23 (11.6)	176 (88.4)	NE (23.3, NE)	95	1 (1.1)	94 (98.9)	NE (NE, NE)	5.9611 (0.7949, 44.7027) 0.0824	0.0488	0.2429
1	172	22 (12.8)	150 (87.2)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE) 0.9913	0.0133	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.4458
0	60	9 (15.0)	51 (85.0)	NE (12.5, NE)	31	0	31 (100)	NE (NE, NE)	NE (NE, NE) 0.9947	0.1382	
1	107	11 (10.3)	96 (89.7)	NE (NE, NE)	48	0	48 (100)	NE (NE, NE)	NE (NE, NE) 0.9932	0.0441	
2	114	14 (12.3)	100 (87.7)	NE (23.3, NE)	50	1 (2.0)	49 (98.0)	NE (NE, NE)	2.8392 (0.3602, 22.3790) 0.3219	0.3007	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	11 (12.2)	79 (87.8)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9943	0.1130	

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 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.3776
PD	173	19 (11.0)	154 (89.0)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE) 0.9921	0.0268	
PR	48	7 (14.6)	41 (85.4)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	NE (NE, NE) 0.9942	0.3264	
SD	82	9 (11.0)	73 (89.0)	23.3 (23.3, NE)	54	1 (1.9)	53 (98.1)	NE (NE, NE)	4.5694 (0.5674, 36.7985) 0.1534	0.1174	

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 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Reported history of CNS metastases											
Yes	37	3 (8.1)	34 (91.9)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (2.0, NE)	0.5125 (0.0494, 5.3204)	0.5691	0.0144
No	334	42 (12.6)	292 (87.4)	NE (23.3, NE)	159	0	159 (100)	NE (NE, NE)	NE (NE, NE)	0.0007	0.9881

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Baseline CNS metastases											0.8523
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.5637	
No	347	44 (12.7)	303 (87.3)	NE (23.3, NE)	165	1 (0.6)	164 (99.4)	NE (NE, NE)	11.7949 (1.6158, 86.0976) 0.0150	0.0020	

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Renal function at baseline											0.3401
Normal Function	201	20 (10.0)	181 (90.0)	NE (23.3, NE)	80	1 (1.3)	79 (98.8)	NE (NE, NE)	4.3064 (0.5675, 32.6775) 0.1579	0.1242	
Mild Impairment	123	15 (12.2)	108 (87.8)	NE (NE, NE)	65	0	65 (100)	NE (NE, NE)	NE (NE, NE) 0.9929	0.0425	
Moderate Impairment	41	9 (22.0)	32 (78.0)	NE (15.2, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9934	0.0422	

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Hepatic function at baseline											0.2454
Normal Function	170	19 (11.2)	151 (88.8)	NE (NE, NE)	88	0	88 (100)	NE (NE, NE)	NE (NE, NE) 0.9915	0.0142	
Mild Impairment	194	26 (13.4)	168 (86.6)	NE (23.3, NE)	82	1 (1.2)	81 (98.8)	NE (NE, NE)	5.7193 (0.7661, 42.6961) 0.0891	0.0550	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
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Baseline visceral disease											
Yes	331	41 (12.4)	290 (87.6)	NE (23.3, NE)	146	1 (0.7)	145 (99.3)	NE (NE, NE)	10.8685 (1.4876, 79.4074) 0.0187	0.0033	0.6577
No	40	4 (10.0)	36 (90.0)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9967	0.3156	

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Hormon receptor status (IXRS)											0.5970
Positive	329	39 (11.9)	290 (88.1)	NE (NE, NE)	152	1 (0.7)	151 (99.3)	NE (NE, NE)	10.5925 (1.4474, 77.5180) 0.0201	0.0038	
Negative	42	6 (14.3)	36 (85.7)	NE (12.5, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) 0.9963	0.2639	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Run date: 13SEP2022 – 17:09; Program name: T4\_TEAE\_2\_SAS.sas; Output name: T4\_AESIILDDRAC\_2\_SAS.rtf

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DE.T.4.15.2 - Adverse events of special interest - Drug-related adjudicated Interstitial lung disease/pneumonitis (ILD) - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (derived)											0.6292
Positive	331	39 (11.8)	292 (88.2)	NE (NE, NE)	155	1 (0.6)	154 (99.4)	NE (NE, NE)	11.0438 (1.5095, 80.7992) 0.0180	0.0030	
Negative	40	6 (15.0)	34 (85.0)	NE (11.1, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) 0.9957	0.4269	

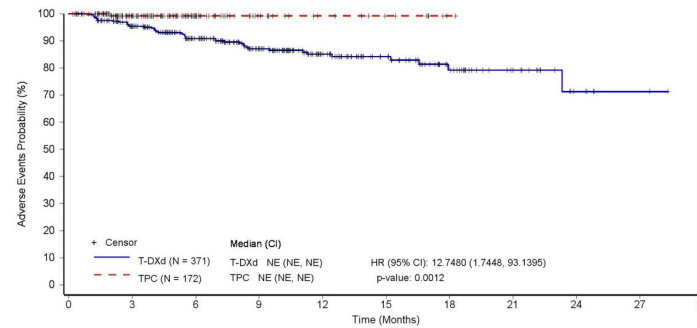
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.15.3 - Adverse events of special interest - Drug-related adjudicated Interstitial lung disease/pneumonitis (ILD) - Kaplan-Meier plot -  
 Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 371)	371	305	229	163	102	68	37	18	6	2	0
TPC (N = 172)	172	106	44	20	11	7	1	0	0	0	0

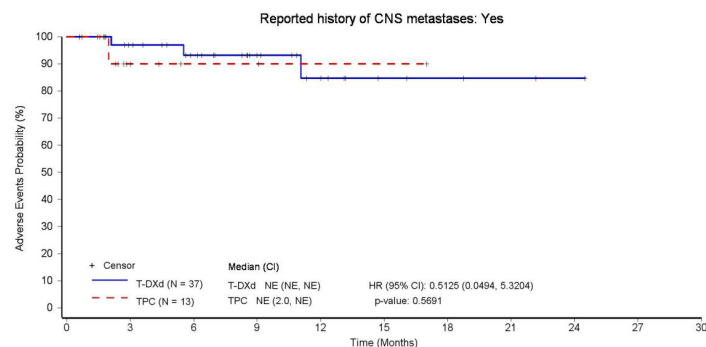
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:12; Program name: F4\_TEAE\_3\_SAS.sas; Output name: F4\_AESIILDDRAC\_3\_SAS.rtf

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DE.F.4.15.4 - Adverse events of special interest - Drug-related adjudicated Interstitial lung disease/pneumonitis (ILD) - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 37)	37	30	23	15	9	4	3	2	1	0	0
TPC (N = 13)	13	5	2	2	1	1	0	0	0	0	0

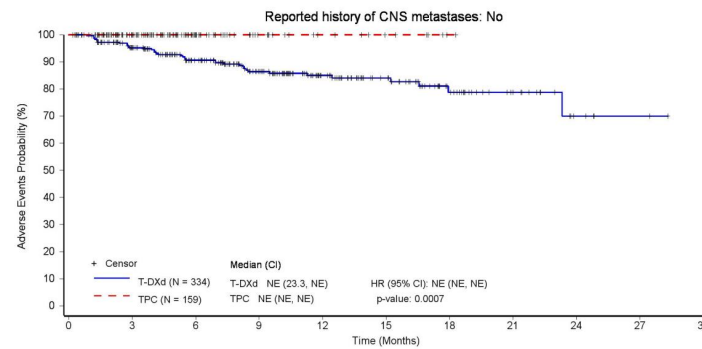
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:12; Program name: F4\_TEAE\_4\_SAS.sas; Output name: F4\_AESIILDRAC\_4\_SAS.rtf

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DE.F.4.15.4 - Adverse events of special interest - Drug-related adjudicated Interstitial lung disease/pneumonitis (ILD) - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 334)	334	275	206	148	93	64	34	16	5	2	0
TPC (N = 159)	159	101	42	18	10	6	1	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.16.1 - Adverse events of special interest - Left ventricular (LV) dysfunction - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	17 (4.6)	0	
Number of subjects censored, n (%)	354 (95.4)	172 (100)	
Median time to first event (months) [a]	NE	NE	
95% Confidence Interval	[NE, NE]	[NE, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			NE
95% Confidence Interval			[NE, NE]
p-value			0.9929
Stratified log-rank p-value [c]			0.0388

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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DE.T.4.16.2 - Adverse events of special interest - Left ventricular (LV) dysfunction - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
HER2 status											1.0000
HER2 IHC 1+	214	10 (4.7)	204 (95.3)	NE (NE, NE)	100	0	100 (100)	NE (NE, NE)	NE (NE, NE) 0.9918	0.1516	
HER2 IHC 2+/ISH Negative	157	7 (4.5)	150 (95.5)	NE (NE, NE)	72	0	72 (100)	NE (NE, NE)	NE (NE, NE) 0.9949	0.1444	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.16.2 - Adverse events of special interest - Left ventricular (LV) dysfunction - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.9996
1	220	14 (6.4)	206 (93.6)	NE (NE, NE)	94	0	94 (100)	NE (NE, NE)	NE (NE, NE) 0.9934	0.0670	
>=2	150	3 (2.0)	147 (98.0)	NE (NE, NE)	78	0	78 (100)	NE (NE, NE)	NE (NE, NE) 0.9967	0.3504	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.16.2 - Adverse events of special interest - Left ventricular (LV) dysfunction - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Prior CDK4/6											NE
Yes	233	11 (4.7)	222 (95.3)	NE (NE, NE)	112	0	112 (100)	NE (NE, NE)	NE (NE, NE) 0.9912	0.1147	
No	98	2 (2.0)	96 (98.0)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9975	0.4924	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.16.2 - Adverse events of special interest - Left ventricular (LV) dysfunction - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											0.9999
<65	289	14 (4.8)	275 (95.2)	NE (NE, NE)	126	0	126 (100)	NE (NE, NE)	NE (NE, NE) 0.9901	0.0816	
>=65	82	3 (3.7)	79 (96.3)	NE (NE, NE)	46	0	46 (100)	NE (NE, NE)	NE (NE, NE) 0.9967	0.3457	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											
<75	357	16 (4.5)	341 (95.5)	NE (NE, NE)	163	0	163 (100)	NE (NE, NE)	NE (NE, NE) 0.9891	0.0509	0.9998
>=75	14	1 (7.1)	13 (92.9)	NE (8.4, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9985	0.4795	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Race											1.0000
White	175	8 (4.6)	167 (95.4)	NE (NE, NE)	85	0	85 (100)	NE (NE, NE)	NE (NE, NE) 0.9929	0.2136	
Non-White	196	9 (4.6)	187 (95.4)	NE (NE, NE)	86	0	86 (100)	NE (NE, NE)	NE (NE, NE) 0.9943	0.1094	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Region											1.0000
Asia	147	3 (2.0)	144 (98.0)	NE (NE, NE)	63	0	63 (100)	NE (NE, NE)	NE (NE, NE) 0.9966	0.3283	
North America	58	5 (8.6)	53 (91.4)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9966	0.3402	
Europe + Israel	166	9 (5.4)	157 (94.6)	NE (NE, NE)	81	0	81 (100)	NE (NE, NE)	NE (NE, NE) 0.9946	0.1310	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
ECOG PS											
0	199	8 (4.0)	191 (96.0)	NE (NE, NE)	95	0	95 (100)	NE (NE, NE)	NE (NE, NE) 0.9950	0.1761	0.9998
1	172	9 (5.2)	163 (94.8)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE) 0.9946	0.1256	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											1.0000
0	60	4 (6.7)	56 (93.3)	NE (NE, NE)	31	0	31 (100)	NE (NE, NE)	NE (NE, NE) 0.9960	0.2403	
1	107	3 (2.8)	104 (97.2)	NE (NE, NE)	48	0	48 (100)	NE (NE, NE)	NE (NE, NE) 0.9967	0.3557	
2	114	6 (5.3)	108 (94.7)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	NE (NE, NE) 0.9945	0.3406	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	4 (4.4)	86 (95.6)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9965	0.3416	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											NE
PD	173	7 (4.0)	166 (96.0)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE) 0.9936	0.2616	
PR	48	5 (10.4)	43 (89.6)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	NE (NE, NE) 0.9963	0.3163	
SD	82	2 (2.4)	80 (97.6)	NE (NE, NE)	54	0	54 (100)	NE (NE, NE)	NE (NE, NE) 0.9967	0.2926	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Reported history of CNS metastases											0.9999
Yes	37	2 (5.4)	35 (94.6)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9979	0.5788	
No	334	15 (4.5)	319 (95.5)	NE (NE, NE)	159	0	159 (100)	NE (NE, NE)	NE (NE, NE) 0.9892	0.0504	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Baseline CNS metastases											
Yes	24	1 (4.2)	23 (95.8)	NE (10.8, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9987	0.7389	1.0000
No	347	16 (4.6)	331 (95.4)	NE (NE, NE)	165	0	165 (100)	NE (NE, NE)	NE (NE, NE) 0.9928	0.0430	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Renal function at baseline											1.0000
Normal Function	201	9 (4.5)	192 (95.5)	NE (NE, NE)	80	0	80 (100)	NE (NE, NE)	NE (NE, NE) 0.9927	0.2035	
Mild Impairment	123	5 (4.1)	118 (95.9)	NE (NE, NE)	65	0	65 (100)	NE (NE, NE)	NE (NE, NE) 0.9956	0.2085	
Moderate Impairment	41	2 (4.9)	39 (95.1)	NE (15.2, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9969	0.3462	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hepatic function at baseline											1.0000
Normal Function	170	9 (5.3)	161 (94.7)	NE (NE, NE)	88	0	88 (100)	NE (NE, NE)	NE (NE, NE) 0.9943	0.1026	
Mild Impairment	194	8 (4.1)	186 (95.9)	NE (NE, NE)	82	0	82 (100)	NE (NE, NE)	NE (NE, NE) 0.9929	0.2104	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Baseline visceral disease											
Yes	331	16 (4.8)	315 (95.2)	NE (NE, NE)	146	0	146 (100)	NE (NE, NE)	NE (NE, NE) 0.9928	0.0451	0.9999
No	40	1 (2.5)	39 (97.5)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9984	0.7995	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (IXRS)											0.9994
Positive	329	13 (4.0)	316 (96.0)	NE (NE, NE)	152	0	152 (100)	NE (NE, NE)	NE (NE, NE) 0.9902	0.0785	
Negative	42	4 (9.5)	38 (90.5)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) 0.9966	0.3199	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (derived)											0.9994
Positive	331	13 (3.9)	318 (96.1)	NE (NE, NE)	155	0	155 (100)	NE (NE, NE)	NE (NE, NE) 0.9936	0.0760	
Negative	40	4 (10.0)	36 (90.0)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) 0.9968	0.3551	

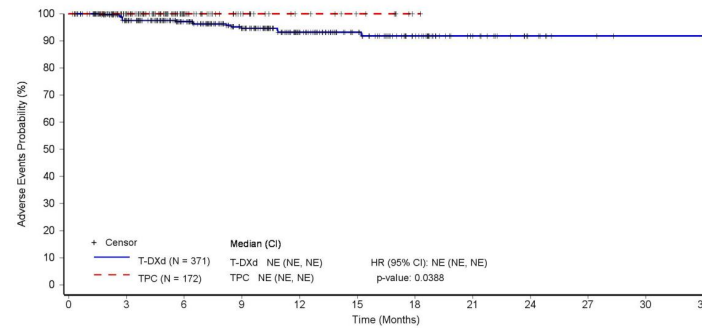
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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 [c] Two-sided p-value from unstratified log-rank test.  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	307	233	170	106	70	42	19	8	3	1	0
TPC (N = 172)	172	107	44	20	11	7	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:12; Program name: F4\_TEAE\_3\_SAS.sas; Output name: F4\_AESILVEF\_3\_SAS.rf

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DE.F.4.16.4 - Adverse events of special interest - Left ventricular (LV) dysfunction - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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No significant interaction has been found

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Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
Run date: 21OCT2022 – 17:12; Program name: F4\_TEAE\_4\_SAS.sas; Output name: F4\_AESILVEF\_4\_SAS.rtf

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DE.T.4.17.1 - Serious Adverse events of special interest - Adjudicated Interstitial lung disease/pneumonitis (ILD) - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	16 (4.3)	1 (0.6)	
Number of subjects censored, n (%)	355 (95.7)	171 (99.4)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			5.0501 [0.6570, 38.8197] 0.1197
Stratified log-rank p-value [c]			0.0845

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:11; Program name: T4\_TEAE\_1\_SAS.sas; Output name: T4\_SAESILLDAC\_1\_SAS.rtf

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DE.T.4.17.2 - Serious Adverse events of special interest - Adjudicated Interstitial lung disease/pneumonitis (ILD) - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
HER2 status											0.2070
HER2 IHC 1+	214	9 (4.2)	205 (95.8)	NE (NE, NE)	100	0	100 (100)	NE (NE, NE)	NE (NE, NE) 0.9943	0.1007	
HER2 IHC 2+/ISH Negative	157	7 (4.5)	150 (95.5)	NE (NE, NE)	72	1 (1.4)	71 (98.6)	NE (NE, NE)	1.8278 (0.2208, 15.1312) 0.5760	0.5704	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:11; Program name: T4\_TEAE\_2\_SAS.sas; Output name: T4\_SAESILLDAC\_2\_SAS.rtf

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DE.T.4.17.2 - Serious Adverse events of special interest - Adjudicated Interstitial lung disease/pneumonitis (ILD) - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.3540
1	220	6 (2.7)	214 (97.3)	NE (NE, NE)	94	0	94 (100)	NE (NE, NE)	NE (NE, NE) 0.9953	0.1883	
>=2	150	10 (6.7)	140 (93.3)	NE (NE, NE)	78	1 (1.3)	77 (98.7)	NE (NE, NE)	2.9134 (0.3649, 23.2590) 0.3130	0.2911	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:11; Program name: T4\_TEAE\_2\_SAS.sas; Output name: T4\_SAESILLDAC\_2\_SAS.rtf

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DE.T.4.17.2 - Serious Adverse events of special interest - Adjudicated Interstitial lung disease/pneumonitis (ILD) - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Prior CDK4/6											
Yes	233	8 (3.4)	225 (96.6)	NE (NE, NE)	112	1 (0.9)	111 (99.1)	NE (NE, NE)	2.2355 (0.2745, 18.2049) 0.4521	0.4403	0.3213
No	98	5 (5.1)	93 (94.9)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9957	0.2156	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Run date: 13SEP2022 – 17:11; Program name: T4\_TEAE\_2\_SAS.sas; Output name: T4\_SAESILLDAC\_2\_SAS.rtf

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											
<65	289	13 (4.5)	276 (95.5)	NE (NE, NE)	126	1 (0.8)	125 (99.2)	NE (NE, NE)	3.0727 (0.3972, 23.7685)	0.2576	0.4401
>=65	82	3 (3.7)	79 (96.3)	NE (NE, NE)	46	0	46 (100)	NE (NE, NE)	NE (NE, NE)	0.2578	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.17.2 - Serious Adverse events of special interest - Adjudicated Interstitial lung disease/pneumonitis (ILD) - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											
<75	357	16 (4.5)	341 (95.5)	NE (NE, NE)	163	1 (0.6)	162 (99.4)	NE (NE, NE)	4.3319 (0.5680, 33.0356)	0.1232	0.9997
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE)	NE	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Race											0.3404
White	175	10 (5.7)	165 (94.3)	NE (NE, NE)	85	1 (1.2)	84 (98.8)	NE (NE, NE)	3.2031 (0.4059, 25.2772) 0.2694	0.2432	
Non-White	196	6 (3.1)	190 (96.9)	NE (NE, NE)	86	0	86 (100)	NE (NE, NE)	NE (NE, NE) 0.9935	0.2521	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.17.2 - Serious Adverse events of special interest - Adjudicated Interstitial lung disease/pneumonitis (ILD) - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]		Hazard Ratio (95% CI) p-value [b]
Region										0.3636
Asia	147	6 (4.1)	141 (95.9)	NE (NE, NE)	63	0	63 (100)	NE (NE, NE)	NE (NE, NE) 0.9958	0.2582
North America	58	5 (8.6)	53 (91.4)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9960	0.2485
Europe + Israel	166	5 (3.0)	161 (97.0)	NE (NE, NE)	81	1 (1.2)	80 (98.8)	NE (NE, NE)	1.8786 (0.2180, 16.1904) 0.5661	0.5598

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
ECOG PS											
0	199	5 (2.5)	194 (97.5)	NE (NE, NE)	95	1 (1.1)	94 (98.9)	NE (NE, NE)	1.6143 (0.1860, 14.0124) 0.6640	0.6611	0.1369
1	172	11 (6.4)	161 (93.6)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE) 0.9941	0.0972	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.3138
0	60	7 (11.7)	53 (88.3)	NE (NE, NE)	31	0	31 (100)	NE (NE, NE)	NE (NE, NE) 0.9951	0.1670	
1	107	4 (3.7)	103 (96.3)	NE (NE, NE)	48	0	48 (100)	NE (NE, NE)	NE (NE, NE) 0.9958	0.2186	
2	114	3 (2.6)	111 (97.4)	NE (NE, NE)	50	1 (2.0)	49 (98.0)	NE (NE, NE)	0.8023 (0.0765, 8.4096) 0.8542	0.8539	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	2 (2.2)	88 (97.8)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9969	0.6079	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:11; Program name: T4\_TEAE\_2\_SAS.sas; Output name: T4\_SAESIILDAC\_2\_SAS.rtf

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.1566
PD	173	12 (6.9)	161 (93.1)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE) 0.9937	0.0753	
PR	48	0	48 (100)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	NE (NE, NE) NE		
SD	82	1 (1.2)	81 (98.8)	NE (NE, NE)	54	1 (1.9)	53 (98.1)	NE (NE, NE)	0.5090 (0.0316, 8.2021) 0.6339	0.6276	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Reported history of CNS metastases											
Yes	37	2 (5.4)	35 (94.6)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (2.0, NE)	0.4139 (0.0351, 4.8790)	0.4702	0.0316
No	334	14 (4.2)	320 (95.8)	NE (NE, NE)	159	0	159 (100)	NE (NE, NE)	NE (NE, NE)	0.0426	0.9929

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Baseline CNS metastases											
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.5637	0.7557
No	347	15 (4.3)	332 (95.7)	NE (NE, NE)	165	1 (0.6)	164 (99.4)	NE (NE, NE)	4.2058 (0.5493, 32.2016) 0.1666	0.1330	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Renal function at baseline											0.3112
Normal Function	201	6 (3.0)	195 (97.0)	NE (NE, NE)	80	1 (1.3)	79 (98.8)	NE (NE, NE)	1.5895 (0.1873, 13.4891) 0.6711	0.6684	
Mild Impairment	123	8 (6.5)	115 (93.5)	NE (NE, NE)	65	0	65 (100)	NE (NE, NE)	NE (NE, NE) 0.9951	0.1657	
Moderate Impairment	41	2 (4.9)	39 (95.1)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9968	0.3253	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hepatic function at baseline										0.1651
Normal Function	170	9 (5.3)	161 (94.7)	NE (NE, NE)	88	0	88 (100)	NE (NE, NE) 0.9941	0.0913	
Mild Impairment	194	7 (3.6)	187 (96.4)	NE (NE, NE)	82	1 (1.2)	81 (98.8)	1.7754 (0.2123, 14.8500) 0.5963	0.5914	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Baseline visceral disease											
Yes	331	13 (3.9)	318 (96.1)	NE (NE, NE)	146	1 (0.7)	145 (99.3)	NE (NE, NE)	3.8948 (0.5054, 30.0137) 0.1919	0.1597	0.5056
No	40	3 (7.5)	37 (92.5)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9976	0.5144	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (IXRS)											
Positive	329	12 (3.6)	317 (96.4)	NE (NE, NE)	152	1 (0.7)	151 (99.3)	NE (NE, NE)	3.2909 (0.4232, 25.5912) 0.2550	0.2279	0.4555
Negative	42	4 (9.5)	38 (90.5)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) 0.9963	0.2639	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:11; Program name: T4\_TEAE\_2\_SAS.sas; Output name: T4\_SAESILLDAC\_2\_SAS.rtf

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (derived)											0.4985
Positive	331	12 (3.6)	319 (96.4)	NE (NE, NE)	155	1 (0.6)	154 (99.4)	NE (NE, NE)	3.6210 (0.4667, 28.0945) 0.2183	0.1882	
Negative	40	4 (10.0)	36 (90.0)	NE (11.1, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) 0.9972	0.4269	

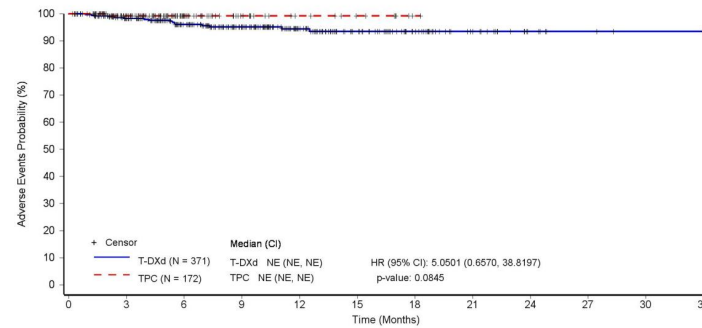
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:11; Program name: T4\_TEAE\_2\_SAS.sas; Output name: T4\_SAESILLDAC\_2\_SAS.rtf

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DE.F.4.17.3 - Serious Adverse events of special interest - Adjudicated Interstitial lung disease/pneumonitis (ILD)) - Kaplan-Meier plot -  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	312	235	172	109	70	41	19	7	3	1	0
TPC (N = 172)	172	106	44	20	11	7	1	0	0	0	0	0

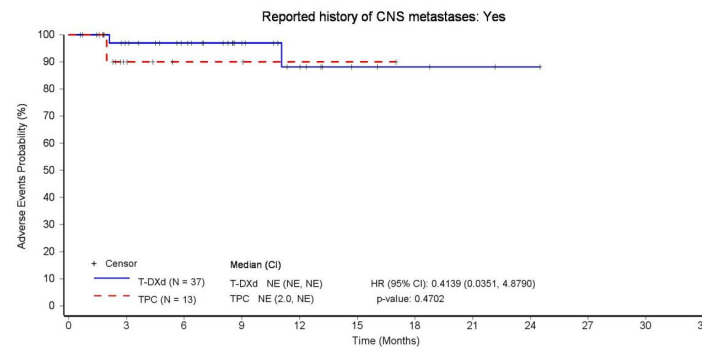
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:12; Program name: F4\_TEAE\_3\_SAS.sas; Output name: F4\_SAESILDAC\_3\_SAS.rtf

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DE.F.4.17.4 - Serious Adverse events of special interest - Adjudicated Interstitial lung disease/pneumonitis (ILD) - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 37)	37	30	24	15	9	4	3	2	1	0	0	0
TPC (N = 13)	13	5	2	2	1	1	0	0	0	0	0	0

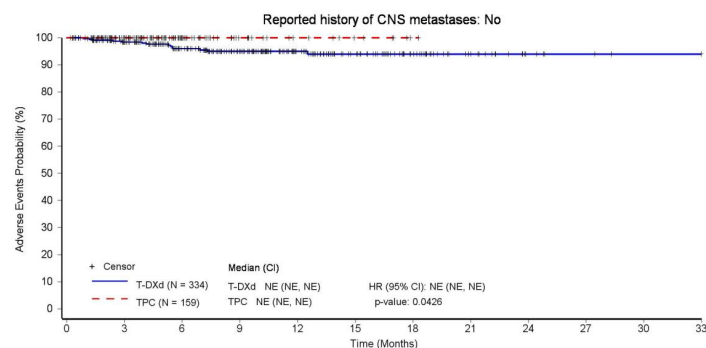
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_TEAE\_4\_SAS.sas; Output name: F4\_SAESILDAC\_4\_SAS.rtf

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DE.F.4.17.4 - Serious Adverse events of special interest - Adjudicated Interstitial lung disease/pneumonitis (ILD) - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 334)	334	282	211	157	100	66	38	17	6	3	1	0
TPC (N = 159)	159	101	42	18	10	6	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_TEAE\_4\_SAS.sas; Output name: F4\_SAESILDAC\_4\_SAS.rf



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DE.T.4.18.1 - Serious Adverse events of special interest - Drug-related adjudicated Interstitial lung disease/pneumonitis (ILD) - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	16 (4.3)	1 (0.6)	
Number of subjects censored, n (%)	355 (95.7)	171 (99.4)	
Median time to first event (months) [a]	NE	NE	
95% Confidence Interval	[NE, NE]	[NE, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			5.0501
95% Confidence Interval			[0.6570, 38.8197]
p-value			0.1197
Stratified log-rank p-value [c]			0.0845

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
HER2 status											0.2070
HER2 IHC 1+	214	9 (4.2)	205 (95.8)	NE (NE, NE)	100	0	100 (100)	NE (NE, NE)	NE (NE, NE) 0.9943	0.1007	
HER2 IHC 2+/ISH Negative	157	7 (4.5)	150 (95.5)	NE (NE, NE)	72	1 (1.4)	71 (98.6)	NE (NE, NE)	1.8278 (0.2208, 15.1312) 0.5760	0.5704	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.3540
1	220	6 (2.7)	214 (97.3)	NE (NE, NE)	94	0	94 (100)	NE (NE, NE)	NE (NE, NE) 0.9953	0.1883	
>=2	150	10 (6.7)	140 (93.3)	NE (NE, NE)	78	1 (1.3)	77 (98.7)	NE (NE, NE)	2.9134 (0.3649, 23.2590) 0.3130	0.2911	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Prior CDK4/6											
Yes	233	8 (3.4)	225 (96.6)	NE (NE, NE)	112	1 (0.9)	111 (99.1)	NE (NE, NE)	2.2355 (0.2745, 18.2049) 0.4521	0.4403	0.3213
No	98	5 (5.1)	93 (94.9)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9957	0.2156	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											
<65	289	13 (4.5)	276 (95.5)	NE (NE, NE)	126	1 (0.8)	125 (99.2)	NE (NE, NE)	3.0727 (0.3972, 23.7685)	0.2576	0.4401
>=65	82	3 (3.7)	79 (96.3)	NE (NE, NE)	46	0	46 (100)	NE (NE, NE)	NE (NE, NE)	0.2578	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											
<75	357	16 (4.5)	341 (95.5)	NE (NE, NE)	163	1 (0.6)	162 (99.4)	NE (NE, NE)	4.3319 (0.5680, 33.0356)	0.1232	0.9997
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE)	NE	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Race											0.3404
White	175	10 (5.7)	165 (94.3)	NE (NE, NE)	85	1 (1.2)	84 (98.8)	NE (NE, NE)	3.2031 (0.4059, 25.2772) 0.2694	0.2432	
Non-White	196	6 (3.1)	190 (96.9)	NE (NE, NE)	86	0	86 (100)	NE (NE, NE)	NE (NE, NE) 0.9935	0.2521	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Region											0.3636
Asia	147	6 (4.1)	141 (95.9)	NE (NE, NE)	63	0	63 (100)	NE (NE, NE)	NE (NE, NE) 0.9958	0.2582	
North America	58	5 (8.6)	53 (91.4)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9960	0.2485	
Europe + Israel	166	5 (3.0)	161 (97.0)	NE (NE, NE)	81	1 (1.2)	80 (98.8)	NE (NE, NE)	1.8786 (0.2180, 16.1904) 0.5661	0.5598	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
ECOG PS											
0	199	5 (2.5)	194 (97.5)	NE (NE, NE)	95	1 (1.1)	94 (98.9)	NE (NE, NE)	1.6143 (0.1860, 14.0124) 0.6640	0.6611	0.1369
1	172	11 (6.4)	161 (93.6)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE) 0.9941	0.0972	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.3138
0	60	7 (11.7)	53 (88.3)	NE (NE, NE)	31	0	31 (100)	NE (NE, NE)	NE (NE, NE) 0.9951	0.1670	
1	107	4 (3.7)	103 (96.3)	NE (NE, NE)	48	0	48 (100)	NE (NE, NE)	NE (NE, NE) 0.9958	0.2186	
2	114	3 (2.6)	111 (97.4)	NE (NE, NE)	50	1 (2.0)	49 (98.0)	NE (NE, NE)	0.8023 (0.0765, 8.4096) 0.8542	0.8539	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	2 (2.2)	88 (97.8)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9969	0.6079	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.1566
PD	173	12 (6.9)	161 (93.1)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE) 0.9937	0.0753	
PR	48	0	48 (100)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	NE (NE, NE) NE		
SD	82	1 (1.2)	81 (98.8)	NE (NE, NE)	54	1 (1.9)	53 (98.1)	NE (NE, NE)	0.5090 (0.0316, 8.2021) 0.6339	0.6276	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:11; Program name: T4\_TEAE\_2\_SAS.sas; Output name: T4\_SAESIILDDRAC\_2\_SAS.rtf

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Reported history of CNS metastases											
Yes	37	2 (5.4)	35 (94.6)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (2.0, NE)	0.4139 (0.0351, 4.8790)	0.4702	0.0316
No	334	14 (4.2)	320 (95.8)	NE (NE, NE)	159	0	159 (100)	NE (NE, NE)	NE (NE, NE)	0.0426	0.9929

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:11; Program name: T4\_TEAE\_2\_SAS.sas; Output name: T4\_SAESILLDDRAC\_2\_SAS.rtf

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Baseline CNS metastases											
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.5637	0.7557
No	347	15 (4.3)	332 (95.7)	NE (NE, NE)	165	1 (0.6)	164 (99.4)	NE (NE, NE)	4.2058 (0.5493, 32.2016) 0.1666	0.1330	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Renal function at baseline											0.3112
Normal Function	201	6 (3.0)	195 (97.0)	NE (NE, NE)	80	1 (1.3)	79 (98.8)	NE (NE, NE)	1.5895 (0.1873, 13.4891) 0.6711	0.6684	
Mild Impairment	123	8 (6.5)	115 (93.5)	NE (NE, NE)	65	0	65 (100)	NE (NE, NE)	NE (NE, NE) 0.9951	0.1657	
Moderate Impairment	41	2 (4.9)	39 (95.1)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9968	0.3253	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Run date: 13SEP2022 – 17:11; Program name: T4\_TEAE\_2\_SAS.sas; Output name: T4\_SAESILLDDRAC\_2\_SAS.rtf

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hepatic function at baseline										0.1651
Normal Function	170	9 (5.3)	161 (94.7)	NE (NE, NE)	88	0	88 (100)	NE (NE, NE) 0.9941	0.0913	
Mild Impairment	194	7 (3.6)	187 (96.4)	NE (NE, NE)	82	1 (1.2)	81 (98.8)	1.7754 (0.2123, 14.8500) 0.5963	0.5914	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Run date: 13SEP2022 – 17:11; Program name: T4\_TEAE\_2\_SAS.sas; Output name: T4\_SAESILLDDRAC\_2\_SAS.rtf



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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Baseline visceral disease											
Yes	331	13 (3.9)	318 (96.1)	NE (NE, NE)	146	1 (0.7)	145 (99.3)	NE (NE, NE)	3.8948 (0.5054, 30.0137) 0.1919	0.1597	0.5056
No	40	3 (7.5)	37 (92.5)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9976	0.5144	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (IXRS)										0.4555
Positive	329	12 (3.6)	317 (96.4)	NE (NE, NE)	152	1 (0.7)	151 (99.3)	3.2909 (0.4232, 25.5912)	0.2279	
Negative	42	4 (9.5)	38 (90.5)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE) 0.9963	0.2639	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:11; Program name: T4\_TEAE\_2\_SAS.sas; Output name: T4\_SAESIIILDDRAC\_2\_SAS.rtf

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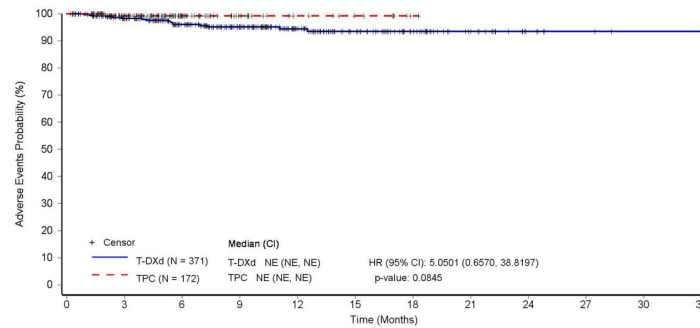
Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (derived)											0.4985
Positive	331	12 (3.6)	319 (96.4)	NE (NE, NE)	155	1 (0.6)	154 (99.4)	NE (NE, NE)	3.6210 (0.4667, 28.0945) 0.2183	0.1882	
Negative	40	4 (10.0)	36 (90.0)	NE (11.1, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) 0.9972	0.4269	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:11; Program name: T4\_TEAE\_2\_SAS.sas; Output name: T4\_SAESILLDDRAC\_2\_SAS.rtf

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 DE.F.4.18.3 - Serious Adverse events of special interest - Drug-related adjudicated Interstitial lung disease/pneumonitis (ILD) - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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Patients still at risk:

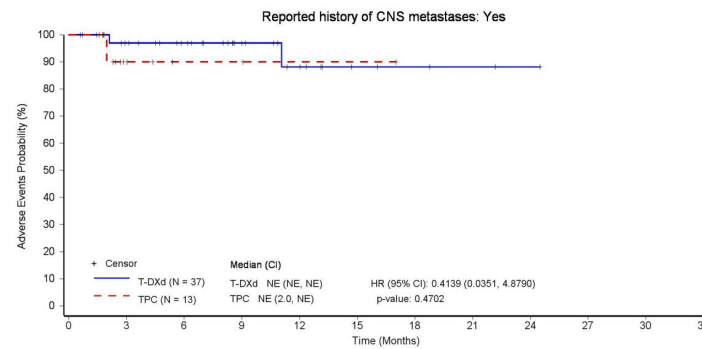
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	312	235	172	109	70	41	19	7	3	1	0
TPC (N = 172)	172	106	44	20	11	7	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

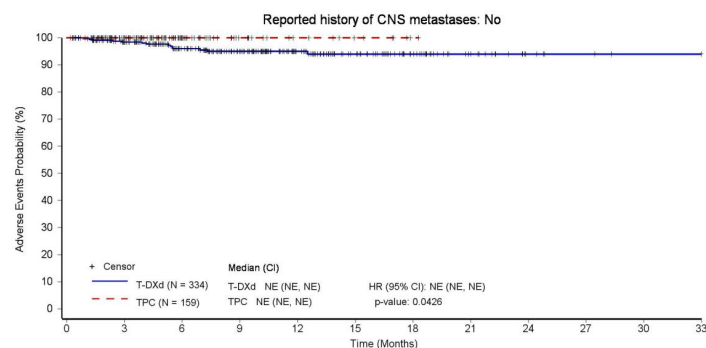
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 37)	37	30	24	15	9	4	3	2	1	0	0	0
TPC (N = 13)	13	5	2	2	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_TEAE\_4\_SAS.sas; Output name: F4\_SAESILDDRAC\_4\_SAS.rtf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 334)	334	282	211	157	100	66	38	17	6	3	1	0
TPC (N = 159)	159	101	42	18	10	6	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_TEAE\_4\_SAS.sas; Output name: F4\_SAESILDDRAC\_4\_SAS.rtf

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DE.T.4.19.1 - Serious Adverse events of special interest - Left ventricular (LV) dysfunction - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	1 (0.3)	0	
Number of subjects censored, n (%)	370 (99.7)	172 (100)	
Median time to first event (months) [a]	NE	NE	
95% Confidence Interval	[NE, NE]	[NE, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			NE
95% Confidence Interval			[NE, NE]
p-value			0.9979
Stratified log-rank p-value [c]			0.5525

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 13SEP2022 – 17:12; Program name: T4\_TEAE\_1\_SAS.sas; Output name: T4\_SAESILVEF\_1\_SAS.rtf

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DE.T.4.19.2 - Serious Adverse events of special interest - Left ventricular (LV) dysfunction - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
HER2 status											NE
HER2 IHC 1+	214	0	214 (100)	NE (NE, NE)	100	0	100 (100)	NE (NE, NE)	NE (NE, NE)		
HER2 IHC 2+/ISH Negative	157	1 (0.6)	156 (99.4)	NE (NE, NE)	72	0	72 (100)	NE (NE, NE)	NE (NE, NE) 0.9979	0.5513	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											NE
1	220	1 (0.5)	219 (99.5)	NE (NE, NE)	94	0	94 (100)	NE (NE, NE)	NE (NE, NE)	0.5586	
>=2	150	0	150 (100)	NE (NE, NE)	78	0	78 (100)	NE (NE, NE)	NE (NE, NE)		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Prior CDK4/6											
Yes	233	1 (0.4)	232 (99.6)	NE (NE, NE)	112	0	112 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.5540	0.9998
No	98	0	98 (100)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											0.9999
<65	289	1 (0.3)	288 (99.7)	NE (NE, NE)	126	0	126 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.5787	
>=65	82	0	82 (100)	NE (NE, NE)	46	0	46 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											
<75	357	1 (0.3)	356 (99.7)	NE (NE, NE)	163	0	163 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.5618	0.9999
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Race											NE
White	175	0	175 (100)	NE (NE, NE)	85	0	85 (100)	NE (NE, NE)	NE (NE, NE)		
Non-White	196	1 (0.5)	195 (99.5)	NE (NE, NE)	86	0	86 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.5604	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Region											1.0000
Asia	147	0	147 (100)	NE (NE, NE)	63	0	63 (100)	NE (NE, NE)	NE (NE, NE)		
North America	58	1 (1.7)	57 (98.3)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE)	0.5518	
Europe + Israel	166	0	166 (100)	NE (NE, NE)	81	0	81 (100)	NE (NE, NE)	NE (NE, NE)		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
ECOG PS											
0	199	0	199 (100)	NE (NE, NE)	95	0	95 (100)	NE (NE, NE)	NE (NE, NE)		NE
1	172	1 (0.6)	171 (99.4)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE) 0.9979	0.5398	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											NE
0	60	0	60 (100)	NE (NE, NE)	31	0	31 (100)	NE (NE, NE)	NE (NE, NE)		
1	107	0	107 (100)	NE (NE, NE)	48	0	48 (100)	NE (NE, NE)	NE (NE, NE)		
2	114	1 (0.9)	113 (99.1)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.5719	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	0	90 (100)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											NE
PD	173	1 (0.6)	172 (99.4)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE)	0.5677	0.9980
PR	48	0	48 (100)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	NE (NE, NE)		NE
SD	82	0	82 (100)	NE (NE, NE)	54	0	54 (100)	NE (NE, NE)	NE (NE, NE)		NE

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Reported history of CNS metastases											NE
Yes	37	1 (2.7)	36 (97.3)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9982	0.6347	
No	334	0	334 (100)	NE (NE, NE)	159	0	159 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.19.2 - Serious Adverse events of special interest - Left ventricular (LV) dysfunction - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Baseline CNS metastases											0.9999
Yes	24	0	24 (100)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE)		
No	347	1 (0.3)	346 (99.7)	NE (NE, NE)	165	0	165 (100)	NE (NE, NE)	NE (NE, NE) 0.9979	0.5517	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.19.2 - Serious Adverse events of special interest - Left ventricular (LV) dysfunction - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Renal function at baseline											NE
Normal Function	201	1 (0.5)	200 (99.5)	NE (NE, NE)	80	0	80 (100)	NE (NE, NE)	NE (NE, NE) 0.9981	0.5867	
Mild Impairment	123	0	123 (100)	NE (NE, NE)	65	0	65 (100)	NE (NE, NE)	NE (NE, NE) NE		
Moderate Impairment	41	0	41 (100)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.19.2 - Serious Adverse events of special interest - Left ventricular (LV) dysfunction - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hepatic function at baseline											NE
Normal Function	170	0	170 (100)	NE (NE, NE)	88	0	88 (100)	NE (NE, NE)	NE (NE, NE)		
Mild Impairment	194	1 (0.5)	193 (99.5)	NE (NE, NE)	82	0	82 (100)	NE (NE, NE)	NE (NE, NE) 0.9981	0.5890	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.19.2 - Serious Adverse events of special interest - Left ventricular (LV) dysfunction - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Baseline visceral disease											
Yes	331	1 (0.3)	330 (99.7)	NE (NE, NE)	146	0	146 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.5589	0.9999
No	40	0	40 (100)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.19.2 - Serious Adverse events of special interest - Left ventricular (LV) dysfunction - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (IXRS)											0.9999
Positive	329	1 (0.3)	328 (99.7)	NE (NE, NE)	152	0	152 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.5577	
Negative	42	0	42 (100)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.19.2 - Serious Adverse events of special interest - Left ventricular (LV) dysfunction - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (derived)											0.9999
Positive	331	1 (0.3)	330 (99.7)	NE (NE, NE)	155	0	155 (100)	NE (NE, NE)	NE (NE, NE) 0.9979	0.5525	
Negative	40	0	40 (100)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) NE		

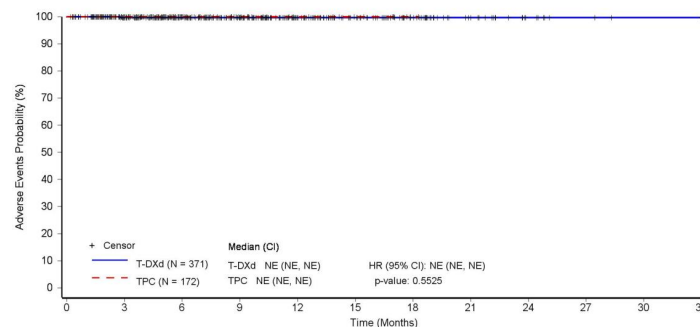
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.19.3 - Serious Adverse events of special interest - Left ventricular (LV) dysfunction - Kaplan-Meier plot - Destiny Breast 04 - DCO  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	313	237	175	111	73	44	20	8	3	1	0
TPC (N = 172)	172	107	44	20	11	7	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_TEAE\_3\_SAS.sas; Output name: F4\_SAESILVEF\_3\_SAS.rf

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No significant interaction has been found

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Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
Run date: 21OCT2022 – 17:13; Program name: F4\_TEAE\_4\_SAS.sas; Output name: F4\_SAESILVEF\_4\_SAS.rtf

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DE.T.4.20.1 - Severe Adverse events of special interest (CTCAE Grade >= 3) - Adjudicated Interstitial lung disease/pneumonitis (ILD) - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	8 (2.2)	0	
Number of subjects censored, n (%)	363 (97.8)	172 (100)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			NE [NE, NE] 0.9945
Stratified log-rank p-value [c]			0.1058

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:12; Program name: T4\_TEAE\_1\_SAS.sas; Output name: T4\_SEVAESIILDAC\_1\_SAS.rtf

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DE.T.4.20.2 - Severe Adverse events of special interest (CTCAE Grade >= 3) - Adjudicated Interstitial lung disease/pneumonitis (ILD) - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
HER2 status											0.9999
HER2 IHC 1+	214	4 (1.9)	210 (98.1)	NE (NE, NE)	100	0	100 (100)	NE (NE, NE)	NE (NE, NE) 0.9962	0.2769	
HER2 IHC 2+/ISH Negative	157	4 (2.5)	153 (97.5)	NE (NE, NE)	72	0	72 (100)	NE (NE, NE)	NE (NE, NE) 0.9965	0.3356	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.20.2 - Severe Adverse events of special interest (CTCAE Grade >= 3) - Adjudicated Interstitial lung disease/pneumonitis (ILD) - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.9997
1	220	3 (1.4)	217 (98.6)	NE (NE, NE)	94	0	94 (100)	NE (NE, NE)	NE (NE, NE) 0.9967	0.3567	
>=2	150	5 (3.3)	145 (96.7)	NE (NE, NE)	78	0	78 (100)	NE (NE, NE)	NE (NE, NE) 0.9959	0.2359	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:12; Program name: T4\_TEAE\_2\_SAS.sas; Output name: T4\_SEVAESIILDAC\_2\_SAS.rtf

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DE.T.4.20.2 - Severe Adverse events of special interest (CTCAE Grade >= 3) - Adjudicated Interstitial lung disease/pneumonitis (ILD) - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Prior CDK4/6											NE
Yes	233	6 (2.6)	227 (97.4)	NE (NE, NE)	112	0	112 (100)	NE (NE, NE)	NE (NE, NE) 0.9954	0.1897	
No	98	1 (1.0)	97 (99.0)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9984	0.6636	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											0.9996
<65	289	8 (2.8)	281 (97.2)	NE (NE, NE)	126	0	126 (100)	NE (NE, NE)	NE (NE, NE) 0.9923	0.1675	
>=65	82	0	82 (100)	NE (NE, NE)	46	0	46 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9998
<75	357	8 (2.2)	349 (97.8)	NE (NE, NE)	163	0	163 (100)	NE (NE, NE)	NE (NE, NE)	0.1538	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE)		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Race											NE
White	175	7 (4.0)	168 (96.0)	NE (NE, NE)	85	0	85 (100)	NE (NE, NE)	NE (NE, NE) 0.9950	0.1546	
Non-White	196	1 (0.5)	195 (99.5)	NE (NE, NE)	86	0	86 (100)	NE (NE, NE)	NE (NE, NE) 0.9979	0.7365	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Region											NE
Asia	147	1 (0.7)	146 (99.3)	NE (NE, NE)	63	0	63 (100)	NE (NE, NE)	NE (NE, NE) 0.9978	0.7237	
North America	58	4 (6.9)	54 (93.1)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9965	0.3152	
Europe + Israel	166	3 (1.8)	163 (98.2)	NE (NE, NE)	81	0	81 (100)	NE (NE, NE)	NE (NE, NE) 0.9966	0.3289	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
ECOG PS											
0	199	2 (1.0)	197 (99.0)	NE (NE, NE)	95	0	95 (100)	NE (NE, NE)	NE (NE, NE) 0.9970	0.3754	NE
1	172	6 (3.5)	166 (96.5)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE) 0.9937	0.2593	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											1.0000
0	60	3 (5.0)	57 (95.0)	NE (NE, NE)	31	0	31 (100)	NE (NE, NE)	NE (NE, NE)	0.4301	0.9971
1	107	2 (1.9)	105 (98.1)	NE (NE, NE)	48	0	48 (100)	NE (NE, NE)	NE (NE, NE)	0.3927	0.9971
2	114	3 (2.6)	111 (97.4)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	NE (NE, NE)	0.3711	0.9969

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	0	90 (100)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE)	NE	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											NE
PD	173	7 (4.0)	166 (96.0)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE)	0.1975	0.9954
PR	48	0	48 (100)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	NE (NE, NE)		NE
SD	82	0	82 (100)	NE (NE, NE)	54	0	54 (100)	NE (NE, NE)	NE (NE, NE)		NE

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.9996
Yes	37	2 (5.4)	35 (94.6)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9977	0.5315	
No	334	6 (1.8)	328 (98.2)	NE (NE, NE)	159	0	159 (100)	NE (NE, NE)	NE (NE, NE) 0.9954	0.1891	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Baseline CNS metastases											0.9998
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.5637	
No	347	7 (2.0)	340 (98.0)	NE (NE, NE)	165	0	165 (100)	NE (NE, NE)	NE (NE, NE) 0.9926	0.1825	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Renal function at baseline											1.0000
Normal Function	201	4 (2.0)	197 (98.0)	NE (NE, NE)	80	0	80 (100)	NE (NE, NE)	NE (NE, NE) 0.9963	0.3039	
Mild Impairment	123	3 (2.4)	120 (97.6)	NE (NE, NE)	65	0	65 (100)	NE (NE, NE)	NE (NE, NE) 0.9962	0.5046	
Moderate Impairment	41	1 (2.4)	40 (97.6)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9977	0.4736	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.9998
Normal Function	170	3 (1.8)	167 (98.2)	NE (NE, NE)	88	0	88 (100)	NE (NE, NE)	NE (NE, NE) 0.9964	0.2965	
Mild Impairment	194	5 (2.6)	189 (97.4)	NE (NE, NE)	82	0	82 (100)	NE (NE, NE)	NE (NE, NE) 0.9943	0.3109	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.20.2 - Severe Adverse events of special interest (CTCAE Grade >= 3) - Adjudicated Interstitial lung disease/pneumonitis (ILD) - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Baseline visceral disease											
Yes	331	7 (2.1)	324 (97.9)	NE (NE, NE)	146	0	146 (100)	NE (NE, NE)	NE (NE, NE) 0.9950	0.1572	1.0000
No	40	1 (2.5)	39 (97.5)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9983	0.7893	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.9995
Positive	329	6 (1.8)	323 (98.2)	NE (NE, NE)	152	0	152 (100)	NE (NE, NE)	NE (NE, NE) 0.9932	0.2238	
Negative	42	2 (4.8)	40 (95.2)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) 0.9971	0.3869	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (derived)											0.9995
Positive	331	6 (1.8)	325 (98.2)	NE (NE, NE)	155	0	155 (100)	NE (NE, NE)	NE (NE, NE) 0.9953	0.1815	
Negative	40	2 (5.0)	38 (95.0)	NE (11.1, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) 0.9974	0.6547	

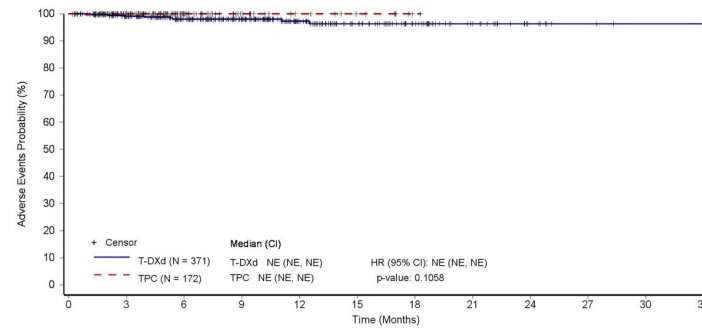
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.F.4.20.3 - Severe Adverse events of special interest (CTCAE Grade >= 3) - Adjudicated Interstitial lung disease/pneumonitis (ILD) - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	313	238	175	111	72	43	20	8	3	1	0
TPC (N = 172)	172	107	44	20	11	7	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_TEAE\_3\_SAS.sas; Output name: F4\_SEVAESILDAC\_3\_SAS.rtf

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DE.F.4.20.4 - Severe Adverse events of special interest (CTCAE Grade  $\geq$  3) - Adjudicated Interstitial lung disease/pneumonitis (ILD) - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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No significant interaction has been found

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Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
Run date: 21OCT2022 – 17:13; Program name: F4\_TEAE\_4\_SAS.sas; Output name: F4\_SEVAESILDAC\_4\_SAS.rtf



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DE.T.4.21.1 - Severe Adverse events of special interest (CTCAE Grade >= 3) - Drug-related adjudicated Interstitial lung disease/pneumonitis (ILD) - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	8 (2.2)	0	
Number of subjects censored, n (%)	363 (97.8)	172 (100)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			NE [NE, NE] 0.9945
Stratified log-rank p-value [c]			0.1058

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:12; Program name: T4\_TEAE\_1\_SAS.sas; Output name: T4\_SEVAESIILDDRAC\_1\_SAS.rtf

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DE.T.4.21.2 - Severe Adverse events of special interest (CTCAE Grade >= 3) - Drug-related adjudicated Interstitial lung disease/pneumonitis (ILD) - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
HER2 status											0.9999
HER2 IHC 1+	214	4 (1.9)	210 (98.1)	NE (NE, NE)	100	0	100 (100)	NE (NE, NE)	NE (NE, NE) 0.9962	0.2769	
HER2 IHC 2+/ISH Negative	157	4 (2.5)	153 (97.5)	NE (NE, NE)	72	0	72 (100)	NE (NE, NE)	NE (NE, NE) 0.9965	0.3356	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.21.2 - Severe Adverse events of special interest (CTCAE Grade >= 3) - Drug-related adjudicated Interstitial lung disease/pneumonitis (ILD) - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.9997
1	220	3 (1.4)	217 (98.6)	NE (NE, NE)	94	0	94 (100)	NE (NE, NE)	NE (NE, NE)	0.3567	0.9967
>=2	150	5 (3.3)	145 (96.7)	NE (NE, NE)	78	0	78 (100)	NE (NE, NE)	NE (NE, NE)	0.2359	0.9959

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Prior CDK4/6											NE
Yes	233	6 (2.6)	227 (97.4)	NE (NE, NE)	112	0	112 (100)	NE (NE, NE)	NE (NE, NE) 0.9954	0.1897	
No	98	1 (1.0)	97 (99.0)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9984	0.6636	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											0.9996
<65	289	8 (2.8)	281 (97.2)	NE (NE, NE)	126	0	126 (100)	NE (NE, NE)	NE (NE, NE) 0.9923	0.1675	
>=65	82	0	82 (100)	NE (NE, NE)	46	0	46 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9998
<75	357	8 (2.2)	349 (97.8)	NE (NE, NE)	163	0	163 (100)	NE (NE, NE)	NE (NE, NE)	0.1538	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE)	NE	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											NE
White	175	7 (4.0)	168 (96.0)	NE (NE, NE)	85	0	85 (100)	NE (NE, NE)	NE (NE, NE) 0.9950	0.1546	
Non-White	196	1 (0.5)	195 (99.5)	NE (NE, NE)	86	0	86 (100)	NE (NE, NE)	NE (NE, NE) 0.9979	0.7365	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Region											NE
Asia	147	1 (0.7)	146 (99.3)	NE (NE, NE)	63	0	63 (100)	NE (NE, NE)	NE (NE, NE) 0.9978	0.7237	
North America	58	4 (6.9)	54 (93.1)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9965	0.3152	
Europe + Israel	166	3 (1.8)	163 (98.2)	NE (NE, NE)	81	0	81 (100)	NE (NE, NE)	NE (NE, NE) 0.9966	0.3289	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
ECOG PS											
0	199	2 (1.0)	197 (99.0)	NE (NE, NE)	95	0	95 (100)	NE (NE, NE)	NE (NE, NE) 0.9970	0.3754	NE
1	172	6 (3.5)	166 (96.5)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE) 0.9937	0.2593	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											1.0000
0	60	3 (5.0)	57 (95.0)	NE (NE, NE)	31	0	31 (100)	NE (NE, NE)	NE (NE, NE)	0.4301	0.9971
1	107	2 (1.9)	105 (98.1)	NE (NE, NE)	48	0	48 (100)	NE (NE, NE)	NE (NE, NE)	0.3927	0.9971
2	114	3 (2.6)	111 (97.4)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	NE (NE, NE)	0.3711	0.9969

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	0	90 (100)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE)	NE	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											NE
PD	173	7 (4.0)	166 (96.0)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE)	0.1975	0.9954
PR	48	0	48 (100)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	NE (NE, NE)		NE
SD	82	0	82 (100)	NE (NE, NE)	54	0	54 (100)	NE (NE, NE)	NE (NE, NE)		NE

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Reported history of CNS metastases											0.9996
Yes	37	2 (5.4)	35 (94.6)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9977	0.5315	
No	334	6 (1.8)	328 (98.2)	NE (NE, NE)	159	0	159 (100)	NE (NE, NE)	NE (NE, NE) 0.9954	0.1891	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.9998
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.5637	
No	347	7 (2.0)	340 (98.0)	NE (NE, NE)	165	0	165 (100)	NE (NE, NE)	NE (NE, NE) 0.9926	0.1825	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Renal function at baseline											1.0000
Normal Function	201	4 (2.0)	197 (98.0)	NE (NE, NE)	80	0	80 (100)	NE (NE, NE)	NE (NE, NE) 0.9963	0.3039	
Mild Impairment	123	3 (2.4)	120 (97.6)	NE (NE, NE)	65	0	65 (100)	NE (NE, NE)	NE (NE, NE) 0.9962	0.5046	
Moderate Impairment	41	1 (2.4)	40 (97.6)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9977	0.4736	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hepatic function at baseline											0.9998
Normal Function	170	3 (1.8)	167 (98.2)	NE (NE, NE)	88	0	88 (100)	NE (NE, NE)	NE (NE, NE) 0.9964	0.2965	
Mild Impairment	194	5 (2.6)	189 (97.4)	NE (NE, NE)	82	0	82 (100)	NE (NE, NE)	NE (NE, NE) 0.9943	0.3109	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Baseline visceral disease											
Yes	331	7 (2.1)	324 (97.9)	NE (NE, NE)	146	0	146 (100)	NE (NE, NE)	NE (NE, NE) 0.9950	0.1572	1.0000
No	40	1 (2.5)	39 (97.5)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9983	0.7893	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.21.2 - Severe Adverse events of special interest (CTCAE Grade >= 3) - Drug-related adjudicated Interstitial lung disease/pneumonitis (ILD) - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.9995
Positive	329	6 (1.8)	323 (98.2)	NE (NE, NE)	152	0	152 (100)	NE (NE, NE)	NE (NE, NE) 0.9932	0.2238	
Negative	42	2 (4.8)	40 (95.2)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) 0.9971	0.3869	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.21.2 - Severe Adverse events of special interest (CTCAE Grade >= 3) - Drug-related adjudicated Interstitial lung disease/pneumonitis (ILD) - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (derived)											0.9995
Positive	331	6 (1.8)	325 (98.2)	NE (NE, NE)	155	0	155 (100)	NE (NE, NE)	NE (NE, NE) 0.9953	0.1815	
Negative	40	2 (5.0)	38 (95.0)	NE (11.1, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) 0.9974	0.6547	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

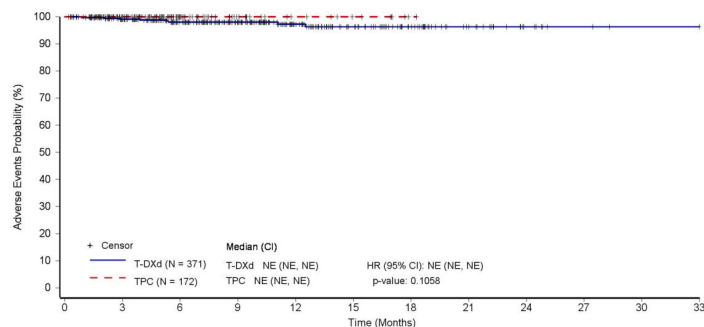
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 DE.F.4.21.3 - Severe Adverse events of special interest (CTCAE Grade >= 3) - Drug-related adjudicated Interstitial lung disease/pneumonitis (ILD) - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	313	238	175	111	72	43	20	8	3	1	0
TPC (N = 172)	172	107	44	20	11	7	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

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DE.F.4.21.4 - Severe Adverse events of special interest (CTCAE Grade  $\geq 3$ ) - Drug-related adjudicated Interstitial lung disease/pneumonitis (ILD) - Kaplan-Meier plot - subgroup analysis  
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No significant interaction has been found

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Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Run date: 21OCT2022 – 17:13; Program name: F4\_TEAE\_4\_SAS.sas; Output name: F4\_SEVAESILDDRAC\_4\_SAS.rtf

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DE.T.4.22.1 - Severe Adverse events of special interest (CTCAE Grade >= 3) - Left ventricular (LV) dysfunction - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	2 (0.5)	0	
Number of subjects censored, n (%)	369 (99.5)	172 (100)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			NE [NE, NE] 0.9979
Stratified log-rank p-value [c]			0.5313

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 13SEP2022 – 17:12; Program name: T4\_TEAE\_1\_SAS.sas; Output name: T4\_SEVAESILVEF\_1\_SAS.rtf

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DE.T.4.22.2 - Severe Adverse events of special interest (CTCAE Grade >= 3) - Left ventricular (LV) dysfunction - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
HER2 status											NE
HER2 IHC 1+	214	2 (0.9)	212 (99.1)	NE (NE, NE)	100	0	100 (100)	NE (NE, NE)	NE (NE, NE) 0.9962	0.4919	
HER2 IHC 2+ /ISH Negative	157	0	157 (100)	NE (NE, NE)	72	0	72 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.22.2 - Severe Adverse events of special interest (CTCAE Grade >= 3) - Left ventricular (LV) dysfunction - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.9998
1	220	2 (0.9)	218 (99.1)	NE (NE, NE)	94	0	94 (100)	NE (NE, NE)	NE (NE, NE)	0.4841	0.9975
>=2	150	0	150 (100)	NE (NE, NE)	78	0	78 (100)	NE (NE, NE)	NE (NE, NE)		NE

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.22.2 - Severe Adverse events of special interest (CTCAE Grade >= 3) - Left ventricular (LV) dysfunction - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Prior CDK4/6											0.9998
Yes	233	1 (0.4)	232 (99.6)	NE (NE, NE)	112	0	112 (100)	NE (NE, NE)	NE (NE, NE) 0.9979	0.5437	
No	98	0	98 (100)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.22.2 - Severe Adverse events of special interest (CTCAE Grade >= 3) - Left ventricular (LV) dysfunction - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											
<65	289	2 (0.7)	287 (99.3)	NE (NE, NE)	126	0	126 (100)	NE (NE, NE)	NE (NE, NE) 0.9964	0.5208	0.9998
>=65	82	0	82 (100)	NE (NE, NE)	46	0	46 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.22.2 - Severe Adverse events of special interest (CTCAE Grade >= 3) - Left ventricular (LV) dysfunction - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9999
<75	357	2 (0.6)	355 (99.4)	NE (NE, NE)	163	0	163 (100)	NE (NE, NE)	NE (NE, NE)	0.4959	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE)	NE	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											1.0000
White	175	1 (0.6)	174 (99.4)	NE (NE, NE)	85	0	85 (100)	NE (NE, NE)	NE (NE, NE) 0.9979	0.7363	
Non-White	196	1 (0.5)	195 (99.5)	NE (NE, NE)	86	0	86 (100)	NE (NE, NE)	NE (NE, NE) 0.9979	0.5506	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											NE
Asia	147	0	147 (100)	NE (NE, NE)	63	0	63 (100)	NE (NE, NE)	NE (NE, NE)		
North America	58	0	58 (100)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE)		
Europe + Israel	166	2 (1.2)	164 (98.8)	NE (NE, NE)	81	0	81 (100)	NE (NE, NE)	NE (NE, NE)	0.4720	0.9974

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.22.2 - Severe Adverse events of special interest (CTCAE Grade >= 3) - Left ventricular (LV) dysfunction - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
ECOG PS											
0	199	1 (0.5)	198 (99.5)	NE (NE, NE)	95	0	95 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.5605	0.9999
1	172	1 (0.6)	171 (99.4)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE) 0.9979	0.7389	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.22.2 - Severe Adverse events of special interest (CTCAE Grade >= 3) - Left ventricular (LV) dysfunction - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											1.0000
0	60	1 (1.7)	59 (98.3)	NE (NE, NE)	31	0	31 (100)	NE (NE, NE)	NE (NE, NE)	0.7237	0.9978
1	107	1 (0.9)	106 (99.1)	NE (NE, NE)	48	0	48 (100)	NE (NE, NE)	NE (NE, NE)	0.5204	0.9979
2	114	0	114 (100)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	NE (NE, NE)		NE

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.22.2 - Severe Adverse events of special interest (CTCAE Grade >= 3) - Left ventricular (LV) dysfunction - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	0	90 (100)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE)	NE	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Run date: 13SEP2022 – 17:12; Program name: T4\_TEAE\_2\_SAS.sas; Output name: T4\_SEVAESILVEF\_2\_SAS.rtf



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DE.T.4.22.2 - Severe Adverse events of special interest (CTCAE Grade >= 3) - Left ventricular (LV) dysfunction - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											NE
PD	173	2 (1.2)	171 (98.8)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE)	0.4994	0.9975
PR	48	0	48 (100)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	NE (NE, NE)		NE
SD	82	0	82 (100)	NE (NE, NE)	54	0	54 (100)	NE (NE, NE)	NE (NE, NE)		NE

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.22.2 - Severe Adverse events of special interest (CTCAE Grade >= 3) - Left ventricular (LV) dysfunction - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.9999
Yes	37	0	37 (100)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE)		
No	334	2 (0.6)	332 (99.4)	NE (NE, NE)	159	0	159 (100)	NE (NE, NE)	NE (NE, NE) 0.9961	0.4793	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.22.2 - Severe Adverse events of special interest (CTCAE Grade >= 3) - Left ventricular (LV) dysfunction - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.9999
Yes	24	0	24 (100)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE)		
No	347	2 (0.6)	345 (99.4)	NE (NE, NE)	165	0	165 (100)	NE (NE, NE)	NE (NE, NE) 0.9961	0.4856	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.22.2 - Severe Adverse events of special interest (CTCAE Grade >= 3) - Left ventricular (LV) dysfunction - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											NE
Normal Function	201	1 (0.5)	200 (99.5)	NE (NE, NE)	80	0	80 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.5807	
Mild Impairment	123	0	123 (100)	NE (NE, NE)	65	0	65 (100)	NE (NE, NE)	NE (NE, NE) NE		
Moderate Impairment	41	0	41 (100)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.22.2 - Severe Adverse events of special interest (CTCAE Grade >= 3) - Left ventricular (LV) dysfunction - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hepatic function at baseline											1.0000
Normal Function	170	1 (0.6)	169 (99.4)	NE (NE, NE)	88	0	88 (100)	NE (NE, NE)	NE (NE, NE) 0.9976	0.6872	
Mild Impairment	194	1 (0.5)	193 (99.5)	NE (NE, NE)	82	0	82 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.5812	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.22.2 - Severe Adverse events of special interest (CTCAE Grade >= 3) - Left ventricular (LV) dysfunction - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.9998
Yes	331	1 (0.3)	330 (99.7)	NE (NE, NE)	146	0	146 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.5536	
No	40	1 (2.5)	39 (97.5)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.8415	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.22.2 - Severe Adverse events of special interest (CTCAE Grade >= 3) - Left ventricular (LV) dysfunction - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (IXRS)											NE
Positive	329	1 (0.3)	328 (99.7)	NE (NE, NE)	152	0	152 (100)	NE (NE, NE)	NE (NE, NE) 0.9979	0.5505	
Negative	42	1 (2.4)	41 (97.6)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	1.0000 (0.0000, ) 1.0000		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.22.2 - Severe Adverse events of special interest (CTCAE Grade >= 3) - Left ventricular (LV) dysfunction - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

Subgroup	T-DXd (N=371)				TPC (N=172)			T-DXd vs TPC		Interaction	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (derived)											NE
Positive	331	1 (0.3)	330 (99.7)	NE (NE, NE)	155	0	155 (100)	NE (NE, NE)	NE (NE, NE) 0.9979	0.5455	
Negative	40	1 (2.5)	39 (97.5)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	1.0000 (0.0000, ) 1.0000		

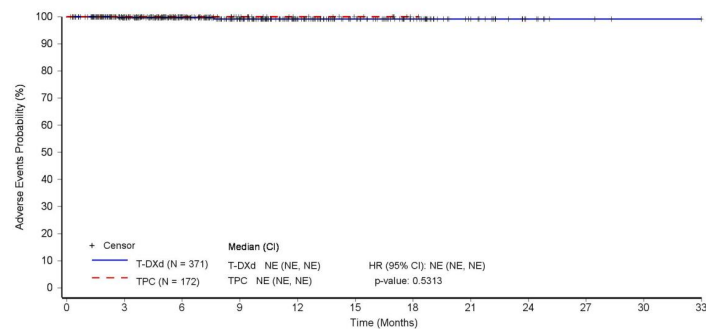
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:12; Program name: T4\_TEAE\_2\_SAS.sas; Output name: T4\_SEVAESILVEF\_2\_SAS.rtf



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 DE.F.4.22.3 - Severe Adverse events of special interest (CTCAE Grade >= 3) - Left ventricular (LV) dysfunction - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	313	238	175	111	73	44	20	8	3	1	0
TPC (N = 172)	172	107	44	20	11	7	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_TEAE\_3\_SAS.sas; Output name: F4\_SEVAESILVEF\_3\_SAS.rtf

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DE.F.4.22.4 - Severe Adverse events of special interest (CTCAE Grade  $\geq 3$ ) - Left ventricular (LV) dysfunction - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO  
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No significant interaction has been found

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Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
Run date: 21OCT2022 – 17:13; Program name: F4\_TEAE\_4\_SAS.sas; Output name: F4\_SEVAESILVEF\_4\_SAS.rtf

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 DE.T.4.23.2 - Non-severe Adverse events of special interest (CTCAE Grade <3) - Adjudicated Interstitial lung disease/pneumonitis (ILD) - Descriptive summary - Destiny Breast 04 - DCO  
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	T-DXd (N=371)	TPC (N=172)
Number of subjects with events, n (%)	39(10.5)	1(0.6)

N: number of subjects in analysis set, n: number of subjects with events; %: proportion of number of subjects in analysis set

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:09; Program name: T4\_AENONSEV\_1\_SAS.sas; Output name: T4\_NSEVAESILDAC\_2\_SAS.rtf

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DE.T.4.24.3 - Non-severe Adverse events of special interest (CTCAE Grade <3) - Drug-related adjudicated Interstitial lung disease/pneumonitis (ILD) - Descriptive summary - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

	T-DXd (N=371)	TPC (N=172)
Number of subjects with events, n (%)	38(10.2)	1(0.6)

N: number of subjects in analysis set, n: number of subjects with events; %: proportion of number of subjects in analysis set

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:09; Program name: T4\_AENONSEV\_1\_SAS.sas; Output name: T4\_NSEVAESILDDRAC\_3\_SAS.rtf

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 DE.T.4.25.4 - Non-severe Adverse events of special interest (CTCAE Grade <3) - Left ventricular (LV) dysfunction - Descriptive summary - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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	T-DXd (N=371)	TPC (N=172)
Number of subjects with events, n (%)	16(4.3)	0

N: number of subjects in analysis set, n: number of subjects with events; %: proportion of number of subjects in analysis set

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:09; Program name: T4\_AENONSEV\_1\_SAS.sas; Output name: T4\_NSEVAESILVEF\_4\_SAS.rtf

**Anhang 4-G 4.3: Unerwünschte Ereignisse nach SOC und PT**

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DE.T.4.7.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	328 (88.4)	117 (68.0)	
Number of subjects censored, n (%)	43 (11.6)	55 (32.0)	
Median time to first event (months) [a]	0.1	0.7	
95% Confidence Interval	[0.1, 0.1]	[0.5, 1.4]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			2.0839
95% Confidence Interval			[1.6774, 2.5888]
p-value			<0.0001
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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DE.T.4.7.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Nausea

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	282 (76.0)	52 (30.2)	
Number of subjects censored, n (%)	89 (24.0)	120 (69.8)	
Median time to first event (months) [a]	0.1	NE	
95% Confidence Interval	[0.1, 0.2]	[11.7, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			3.9712
95% Confidence Interval			[2.9469, 5.3516]
p-value			<0.0001
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 13SEP2022 – 17:13; Program name: T4\_AESOCPT10PER\_1\_SAS.sas; Output name: T4\_AESOCPT10PER\_1\_SAS.rtf



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DE.T.4.7.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Vomiting

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	150 (40.4)	23 (13.4)	
Number of subjects censored, n (%)	221 (59.6)	149 (86.6)	
Median time to first event (months) [a]	NE	NE	
95% Confidence Interval	[10.6, NE]	[NE, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			3.1400
95% Confidence Interval			[2.0200, 4.8808]
p-value			<0.0001
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:13; Program name: T4\_AESOCPT10PER\_1\_SAS.sas; Output name: T4\_AESOCPT10PER\_1\_SAS.rtf

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DE.T.4.7.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Constipation

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	126 (34.0)	38 (22.1)	
Number of subjects censored, n (%)	245 (66.0)	134 (77.9)	
Median time to first event (months) [a] 95% Confidence Interval	NE [17.3, NE]	NE [10.9, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.3871 [0.9607, 2.0026] 0.0808
Stratified log-rank p-value [c]			0.0807

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.7.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Diarrhoea

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	100 (27.0)	38 (22.1)	
Number of subjects censored, n (%)	271 (73.0)	134 (77.9)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.1163 [0.7644, 1.6304] 0.5690
Stratified log-rank p-value [c]			0.5727

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:13; Program name: T4\_AESOCPT10PER\_1\_SAS.sas; Output name: T4\_AESOCPT10PER\_1\_SAS.rtf

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DE.T.4.7.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Stomatitis

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	41 (11.1)	17 (9.9)	
Number of subjects censored, n (%)	330 (88.9)	155 (90.1)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.8472 [0.4777, 1.5027] 0.5707
Stratified log-rank p-value [c]			0.5718

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:13; Program name: T4\_AESOCPT10PER\_1\_SAS.sas; Output name: T4\_AESOCPT10PER\_1\_SAS.rtf

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DE.T.4.7.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	251 (67.7)	114 (66.3)	
Number of subjects censored, n (%)	120 (32.3)	58 (33.7)	
Median time to first event (months) [a]	3.0	0.7	
95% Confidence Interval	[2.2, 4.1]	[0.5, 1.4]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.7105
95% Confidence Interval			[0.5659, 0.8920]
p-value			0.0032
Stratified log-rank p-value [c]			0.0030

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:13; Program name: T4\_AESOCPT10PER\_1\_SAS.sas; Output name: T4\_AESOCPT10PER\_1\_SAS.rtf

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DE.T.4.7.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Aspartate aminotransferase increased

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	92 (24.8)	42 (24.4)	
Number of subjects censored, n (%)	279 (75.2)	130 (75.6)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [13.6, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.7891 [0.5422, 1.1485] 0.2161
Stratified log-rank p-value [c]			0.2124

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:13; Program name: T4\_AESOCPT10PER\_1\_SAS.sas; Output name: T4\_AESOCPT10PER\_1\_SAS.rtf

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DE.T.4.7.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence  $\geq 10\%$  in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Neutrophil count decreased

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	81 (21.8)	62 (36.0)	
Number of subjects censored, n (%)	290 (78.2)	110 (64.0)	
Median time to first event (months) [a]	24.8	NE	
95% Confidence Interval	[24.8, NE]	[6.9, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.4034
95% Confidence Interval			[0.2871, 0.5669]
p-value			<0.0001
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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DE.T.4.7.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: White blood cell count decreased

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	78 (21.0)	49 (28.5)	
Number of subjects censored, n (%)	293 (79.0)	123 (71.5)	
Median time to first event (months) [a] 95% Confidence Interval	24.8 [24.8, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.5252 [0.3641, 0.7574] 0.0006
Stratified log-rank p-value [c]			0.0005

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:13; Program name: T4\_AESOCPT10PER\_1\_SAS.sas; Output name: T4\_AESOCPT10PER\_1\_SAS.rtf



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DE.T.4.7.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Alanine aminotransferase increased

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	75 (20.2)	43 (25.0)	
Number of subjects censored, n (%)	296 (79.8)	129 (75.0)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [13.6, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.6585 [0.4493, 0.9650] 0.0321
Stratified log-rank p-value [c]			0.0315

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.7.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Platelet count decreased

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	73 (19.7)	12 (7.0)	
Number of subjects censored, n (%)	298 (80.3)	160 (93.0)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			2.3530 [1.2708, 4.3568] 0.0065
Stratified log-rank p-value [c]			0.0054

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.7.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Weight decreased

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	60 (16.2)	14 (8.1)	
Number of subjects censored, n (%)	311 (83.8)	158 (91.9)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.3193 [0.7291, 2.3870] 0.3598
Stratified log-rank p-value [c]			0.3594

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.7.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: General disorders and administration site conditions; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	248 (66.8)	102 (59.3)	
Number of subjects censored, n (%)	123 (33.2)	70 (40.7)	
Median time to first event (months) [a]	2.1	1.4	
95% Confidence Interval	[1.3, 3.4]	[0.7, 3.3]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.9693
95% Confidence Interval			[0.7662, 1.2262]
p-value			0.7947
Stratified log-rank p-value [c]			0.7786

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: General disorders and administration site conditions; PT: Fatigue

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	110 (29.6)	50 (29.1)	
Number of subjects censored, n (%)	261 (70.4)	122 (70.9)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.8950 [0.6374, 1.2568] 0.5220
Stratified log-rank p-value [c]			0.5086

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: General disorders and administration site conditions; PT: Asthenia

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	70 (18.9)	25 (14.5)	
Number of subjects censored, n (%)	301 (81.1)	147 (85.5)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.1539 [0.7263, 1.8333] 0.5445
Stratified log-rank p-value [c]			0.5569

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: General disorders and administration site conditions; PT: Pyrexia

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	46 (12.4)	22 (12.8)	
Number of subjects censored, n (%)	325 (87.6)	150 (87.2)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.5691 [0.3341, 0.9694] 0.0381
Stratified log-rank p-value [c]			0.0354

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Skin and subcutaneous tissue disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	195 (52.6)	92 (53.5)	
Number of subjects censored, n (%)	176 (47.4)	80 (46.5)	
Median time to first event (months) [a]	5.7	2.6	
95% Confidence Interval	[3.5, 8.2]	[1.1, 4.2]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.7094
95% Confidence Interval			[0.5504, 0.9145]
p-value			0.0081
Stratified log-rank p-value [c]			0.0076

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	147 (39.6)	57 (33.1)	
Number of subjects censored, n (%)	224 (60.4)	115 (66.9)	
Median time to first event (months) [a] 95% Confidence Interval	NE [16.0, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.0193 [0.7486, 1.3879] 0.9034
Stratified log-rank p-value [c]			0.9122

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.7.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysesthesia syndrome

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	5 (1.3)	24 (14.0)	
Number of subjects censored, n (%)	366 (98.7)	148 (86.0)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.0690 [0.0258, 0.1848] <0.0001
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Metabolism and nutrition disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	188 (50.7)	63 (36.6)	
Number of subjects censored, n (%)	183 (49.3)	109 (63.4)	
Median time to first event (months) [a]	7.2	NE	
95% Confidence Interval	[4.8, 11.8]	[6.5, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			1.3127
95% Confidence Interval			[0.9829, 1.7531]
p-value			0.0653
Stratified log-rank p-value [c]			0.0684

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.7.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Metabolism and nutrition disorders; PT: Decreased appetite

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	118 (31.8)	33 (19.2)	
Number of subjects censored, n (%)	253 (68.2)	139 (80.8)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.6305 [1.1047, 2.4067] 0.0139
Stratified log-rank p-value [c]			0.0135

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	39 (10.5)	12 (7.0)	
Number of subjects censored, n (%)	332 (89.5)	160 (93.0)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.1483 [0.5950, 2.2163] 0.6801
Stratified log-rank p-value [c]			0.6822

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Blood and lymphatic system disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	179 (48.2)	74 (43.0)	
Number of subjects censored, n (%)	192 (51.8)	98 (57.0)	
Median time to first event (months) [a]	9.0	7.0	
95% Confidence Interval	[7.2, 12.0]	[4.1, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.7908
95% Confidence Interval			[0.5987, 1.0445]
p-value			0.0983
Stratified log-rank p-value [c]			0.0979

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.7.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Anaemia

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	139 (37.5)	45 (26.2)	
Number of subjects censored, n (%)	232 (62.5)	127 (73.8)	
Median time to first event (months) [a] 95% Confidence Interval	24.8 [11.7, NE]	NE [15.4, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.0799 [0.7653, 1.5239] 0.6616
Stratified log-rank p-value [c]			0.6712

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.7.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Neutropenia

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	49 (13.2)	31 (18.0)	
Number of subjects censored, n (%)	322 (86.8)	141 (82.0)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.5584 [0.3523, 0.8850] 0.0131
Stratified log-rank p-value [c]			0.0122

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.7.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	155 (41.8)	50 (29.1)	
Number of subjects censored, n (%)	216 (58.2)	122 (70.9)	
Median time to first event (months) [a]	14.3	NE	
95% Confidence Interval	[11.8, 17.9]	[NE, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			1.0256
95% Confidence Interval			[0.7394, 1.4227]
p-value			0.8795
Stratified log-rank p-value [c]			0.8703

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.7.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	39 (10.5)	2 (1.2)	
Number of subjects censored, n (%)	332 (89.5)	170 (98.8)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			5.0895 [1.2150, 21.3202] 0.0260
Stratified log-rank p-value [c]			0.0134

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.7.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence &gt;= 10% in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	38 (10.2)	16 (9.3)	
Number of subjects censored, n (%)	333 (89.8)	156 (90.7)	
Median time to first event (months) [a]	NE	NE	
95% Confidence Interval	[24.4, NE]	[NE, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.8887
95% Confidence Interval			[0.4892, 1.6146]
p-value			0.6986
Stratified log-rank p-value [c]			0.6973

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.7.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Nervous system disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	146 (39.4)	75 (43.6)	
Number of subjects censored, n (%)	225 (60.6)	97 (56.4)	
Median time to first event (months) [a]	18.1	5.0	
95% Confidence Interval	[11.0, NE]	[3.0, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.6166
95% Confidence Interval			[0.4617, 0.8235]
p-value			0.0011
Stratified log-rank p-value [c]			0.0009

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Nervous system disorders; PT: Headache

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	54 (14.6)	11 (6.4)	
Number of subjects censored, n (%)	317 (85.4)	161 (93.6)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.8056 [0.9369, 3.4797] 0.0775
Stratified log-rank p-value [c]			0.0731

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.7.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	18 (4.9)	19 (11.0)	
Number of subjects censored, n (%)	353 (95.1)	153 (89.0)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.3367 [0.1748, 0.6487] 0.0011
Stratified log-rank p-value [c]			0.0007

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.7.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	136 (36.7)	56 (32.6)	
Number of subjects censored, n (%)	235 (63.3)	116 (67.4)	
Median time to first event (months) [a]	16.5	11.0	
95% Confidence Interval	[12.1, NE]	[6.1, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.7321
95% Confidence Interval			[0.5301, 1.0109]
p-value			0.0582
Stratified log-rank p-value [c]			0.0574

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.7.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	43 (11.6)	20 (11.6)	
Number of subjects censored, n (%)	328 (88.4)	152 (88.4)	
Median time to first event (months) [a] 95% Confidence Interval	NE [22.7, NE]	NE [11.5, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.5833 [0.3352, 1.0152] 0.0566
Stratified log-rank p-value [c]			0.0539

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.7.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Infections and infestations; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	127 (34.2)	36 (20.9)	
Number of subjects censored, n (%)	244 (65.8)	136 (79.1)	
Median time to first event (months) [a]	18.0	NE	
95% Confidence Interval	[12.4, NE]	[NE, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			1.1578
95% Confidence Interval			[0.7921, 1.6924]
p-value			0.4493
Stratified log-rank p-value [c]			0.4512

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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DE.T.4.7.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Eye disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	60 (16.2)	21 (12.2)	
Number of subjects censored, n (%)	311 (83.8)	151 (87.8)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [11.3, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.8508 [0.5080, 1.4249] 0.5390
Stratified log-rank p-value [c]			0.5367

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.7.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Psychiatric disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	47 (12.7)	16 (9.3)	
Number of subjects censored, n (%)	324 (87.3)	156 (90.7)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.0497 [0.5897, 1.8686] 0.8690
Stratified log-rank p-value [c]			0.8662

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.7.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Injury, poisoning and procedural complications; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	44 (11.9)	29 (16.9)	
Number of subjects censored, n (%)	327 (88.1)	143 (83.1)	
Median time to first event (months) [a] 95% Confidence Interval	NE [23.9, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.3769 [0.2293, 0.6196] 0.0001
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.7.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Vascular disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	43 (11.6)	19 (11.0)	
Number of subjects censored, n (%)	328 (88.4)	153 (89.0)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.7361 [0.4215, 1.2853] 0.2813
Stratified log-rank p-value [c]			0.2819

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.5580
HER2 IHC 1+	214	193 (90.2)	21 (9.8)	0.1 (0.1, 0.1)	100	66 (66.0)	34 (34.0)	0.9 (0.4, 2.2)	2.1575 (1.6255, 2.8636) <0.0001	<0.0001	
HER2 IHC 2+/ISH Negative	157	135 (86.0)	22 (14.0)	0.1 (0.1, 0.1)	72	51 (70.8)	21 (29.2)	0.5 (0.3, 1.6)	1.8830 (1.3609, 2.6054) 0.0001	0.0002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.9637
1	220	198 (90.0)	22 (10.0)	0.1 (0.1, 0.1)	94	66 (70.2)	28 (29.8)	0.6 (0.4, 1.5)	2.0800 (1.5692, 2.7570) <0.0001	<0.0001	
>=2	150	129 (86.0)	21 (14.0)	0.1 (0.1, 0.1)	78	51 (65.4)	27 (34.6)	1.1 (0.3, 4.9)	1.9713 (1.4211, 2.7345) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											
Yes	233	207 (88.8)	26 (11.2)	0.1 (0.1, 0.1)	112	74 (66.1)	38 (33.9)	0.6 (0.4, 1.4)	2.0610 (1.5761, 2.6950) <0.0001	<0.0001	0.8304
No	98	88 (89.8)	10 (10.2)	0.1 (0.1, 0.1)	43	30 (69.8)	13 (30.2)	0.8 (0.3, 2.7)	2.1548 (1.4152, 3.2810) 0.0003	0.0004	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2911
<65	289	255 (88.2)	34 (11.8)	0.1 (0.1, 0.1)	126	81 (64.3)	45 (35.7)	0.9 (0.5, 2.1)	2.1808 (1.6938, 2.8078) <0.0001	<0.0001	
>=65	82	73 (89.0)	9 (11.0)	0.1 (0.1, 0.1)	46	36 (78.3)	10 (21.7)	0.4 (0.2, 1.5)	1.7104 (1.1418, 2.5621) 0.0092	0.0120	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8411
<75	357	316 (88.5)	41 (11.5)	0.1 (0.1, 0.1)	163	111 (68.1)	52 (31.9)	0.6 (0.4, 1.4)	2.0365 (1.6367, 2.5340) <0.0001	<0.0001	
>=75	14	12 (85.7)	2 (14.3)	0.5 (0.1, 2.0)	9	6 (66.7)	3 (33.3)	4.9 (0.0, 11.7)	2.3004 (0.7948, 6.6578) 0.1244	0.1181	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.2333
White	175	151 (86.3)	24 (13.7)	0.1 (0.1, 0.1)	85	58 (68.2)	27 (31.8)	0.5 (0.4, 1.3)	1.7883 (1.3181, 2.4263) 0.0002	0.0002	
Non-White	196	177 (90.3)	19 (9.7)	0.1 (0.1, 0.1)	86	59 (68.6)	27 (31.4)	1.2 (0.3, 2.4)	2.2496 (1.6688, 3.0327) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence  $\geq$  10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.9541
Asia	147	131 (89.1)	16 (10.9)	0.1 (0.1, 0.1)	63	43 (68.3)	20 (31.7)	0.7 (0.3, 2.2)	2.1033 (1.4850, 2.9792) <0.0001	<0.0001	
North America	58	52 (89.7)	6 (10.3)	0.1 (0.1, 0.2)	28	20 (71.4)	8 (28.6)	0.5 (0.3, 1.4)	2.1848 (1.2841, 3.7171) 0.0039	0.0039	
Europe + Israel	166	145 (87.3)	21 (12.7)	0.1 (0.1, 0.1)	81	54 (66.7)	27 (33.3)	1.0 (0.4, 2.8)	1.9549 (1.4252, 2.6814) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											
0	199	177 (88.9)	22 (11.1)	0.1 (0.1, 0.1)	95	63 (66.3)	32 (33.7)	0.7 (0.4, 2.0)	2.1112 (1.5790, 2.8227) <0.0001	<0.0001	0.7385
1	172	151 (87.8)	21 (12.2)	0.1 (0.1, 0.1)	77	54 (70.1)	23 (29.9)	0.6 (0.3, 2.1)	1.9379 (1.4147, 2.6545) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.9284
0	60	50 (83.3)	10 (16.7)	0.1 (0.1, 0.2)	31	21 (67.7)	10 (32.3)	0.7 (0.2, 4.9)	1.6618 (0.9941, 2.7782) 0.0527	0.0560	
1	107	95 (88.8)	12 (11.2)	0.1 (0.1, 0.1)	48	34 (70.8)	14 (29.2)	0.7 (0.4, 1.6)	2.2033 (1.4807, 3.2784) 0.0001	<0.0001	
2	114	100 (87.7)	14 (12.3)	0.1 (0.1, 0.1)	50	32 (64.0)	18 (36.0)	1.2 (0.3, 5.4)	2.0933 (1.3989, 3.1324) 0.0003	0.0003	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 (92.2)	7 (7.8)	0.1 (0.1, 0.1)	43 (69.8)	13 (30.2)	0.5 (0.3, 2.0)	2.1812 (1.4294, 3.3285) 0.0003	0.0003	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.1330
PD	173	150 (86.7)	23 (13.3)	0.1 (0.1, 0.1)	77	45 (58.4)	32 (41.6)	2.5 (1.1, 5.4)	2.4382 (1.7389, 3.4185) <0.0001	<0.0001	
PR	48	41 (85.4)	7 (14.6)	0.1 (0.1, 0.2)	21	13 (61.9)	8 (38.1)	0.5 (0.2, NE)	2.1861 (1.1668, 4.0960) 0.0146	0.0148	
SD	82	76 (92.7)	6 (7.3)	0.1 (0.1, 0.2)	54	44 (81.5)	10 (18.5)	0.5 (0.3, 0.8)	1.5689 (1.0790, 2.2811) 0.0184	0.0215	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.5723
Yes	37	31 (83.8)	6 (16.2)	0.1 (0.1, 0.3)	13	10 (76.9)	3 (23.1)	0.8 (0.1, 2.8)	1.7650 (0.8579, 3.6309)	0.1249	
No	334	297 (88.9)	37 (11.1)	0.1 (0.1, 0.1)	159	107 (67.3)	52 (32.7)	0.6 (0.4, 1.6)	2.0655 (1.6521, 2.5824)	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.1214
Yes	24	17 (70.8)	7 (29.2)	0.2 (0.1, 1.5)	7	6 (85.7)	1 (14.3)	0.8 (0.1, 1.4)	0.9561 (0.3748, 2.4388)	0.9251	0.8970
No	347	311 (89.6)	36 (10.4)	0.1 (0.1, 0.1)	165	111 (67.3)	54 (32.7)	0.6 (0.5, 1.6)	2.1335 (1.7135, 2.6565)	<0.0001	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.5833
Normal Function	201	172 (85.6)	29 (14.4)	0.1 (0.1, 0.1)	80	49 (61.3)	31 (38.8)	0.9 (0.5, 4.2)	2.1295 (1.5453, 2.9345) <0.0001	<0.0001	
Mild Impairment	123	115 (93.5)	8 (6.5)	0.1 (0.1, 0.1)	65	51 (78.5)	14 (21.5)	0.5 (0.3, 1.1)	2.0374 (1.4586, 2.8459) <0.0001	<0.0001	
Moderate Impairment	41	35 (85.4)	6 (14.6)	0.4 (0.1, 0.7)	23	16 (69.6)	7 (30.4)	1.2 (0.2, 11.7)	1.5291 (0.8402, 2.7828) 0.1645	0.1629	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.4005
Normal Function	170	153 (90.0)	17 (10.0)	0.1 (0.1, 0.1)	88	61 (69.3)	27 (30.7)	1.0 (0.4, 2.2)	2.1395 (1.5838, 2.8902) <0.0001	<0.0001	
Mild Impairment	194	168 (86.6)	26 (13.4)	0.1 (0.1, 0.1)	82	56 (68.3)	26 (31.7)	0.5 (0.3, 1.4)	1.8429 (1.3585, 2.5000) 0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.6889
Yes	331	292 (88.2)	39 (11.8)	0.1 (0.1, 0.1)	146	100 (68.5)	46 (31.5)	0.8 (0.4, 1.5)	2.0061 (1.5946, 2.5237) <0.0001	<0.0001	
No	40	36 (90.0)	4 (10.0)	0.1 (0.1, 0.1)	26	17 (65.4)	9 (34.6)	0.6 (0.3, 5.0)	2.1814 (1.2132, 3.9221) 0.0092	0.0098	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.3759
Positive	329	292 (88.8)	37 (11.2)	0.1 (0.1, 0.1)	152	101 (66.4)	51 (33.6)	0.7 (0.5, 1.5)	2.1059 (1.6752, 2.6472) <0.0001	<0.0001	
Negative	42	36 (85.7)	6 (14.3)	0.1 (0.1, 0.3)	20	16 (80.0)	4 (20.0)	0.6 (0.1, 4.9)	1.6246 (0.8955, 2.9470) 0.1103	0.1171	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.6612
Positive	331	294 (88.8)	37 (11.2)	0.1 (0.1, 0.1)	155	104 (67.1)	51 (32.9)	0.6 (0.4, 1.5)	2.0756 (1.6557, 2.6021)	<0.0001	
Negative	40	34 (85.0)	6 (15.0)	0.1 (0.1, 0.3)	17	13 (76.5)	4 (23.5)	0.7 (0.1, 4.9)	1.7634 (0.9227, 3.3701)	0.0861	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.6089
HER2 IHC 1+	214	165 (77.1)	49 (22.9)	0.1 (0.1, 0.2)	100	29 (29.0)	71 (71.0)	NE (8.2, NE)	4.3135 (2.8994, 6.4175) <0.0001	<0.0001	
HER2 IHC 2+/ISH Negative	157	117 (74.5)	40 (25.5)	0.1 (0.1, 0.2)	72	23 (31.9)	49 (68.1)	NE (6.0, NE)	3.6065 (2.3004, 5.6541) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting									0.4940
1	220 (76.8)	169 (23.2)	0.1 (0.1, 0.2)	94 (34.0)	32 (66.0)	NE (6.0, NE)	3.6871 (2.5201, 5.3943) <0.0001	<0.0001	
>=2	150 (74.7)	112 (25.3)	0.1 (0.1, 0.5)	78 (25.6)	20 (74.4)	NE (11.7, NE)	4.4688 (2.7701, 7.2090) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.5381
Yes	233	177 (76.0)	56 (24.0)	0.1 (0.1, 0.2)	112	34 (30.4)	78 (69.6)	NE (6.0, NE)	3.9116 (2.7037, 5.6591) <0.0001	<0.0001	
No	98	78 (79.6)	20 (20.4)	0.1 (0.1, 0.2)	43	12 (27.9)	31 (72.1)	NE (11.7, NE)	4.7305 (2.5655, 8.7227) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1084
<65	289	221 (76.5)	68 (23.5)	0.1 (0.1, 0.2)	126	33 (26.2)	93 (73.8)	NE (NE, NE)	4.6518 (3.2197, 6.7210) <0.0001	<0.0001	
>=65	82	61 (74.4)	21 (25.6)	0.2 (0.1, 0.7)	46	19 (41.3)	27 (58.7)	8.2 (1.7, NE)	2.8150 (1.6767, 4.7263) 0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7437
<75	357	271 (75.9)	86 (24.1)	0.1 (0.1, 0.2)	163	50 (30.7)	113 (69.3)	NE (8.2, NE)	3.9508 (2.9164, 5.3521) <0.0001	<0.0001	
>=75	14	11 (78.6)	3 (21.4)	0.7 (0.1, 2.8)	9	2 (22.2)	7 (77.8)	NE (0.0, NE)	10.5178 (1.3442, 82.2980) 0.0250	0.0054	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.0427
White	175	127 (72.6)	48 (27.4)	0.2 (0.1, 0.4)	85	30 (35.3)	55 (64.7)	NE (NE, NE)	3.0306 (2.0316, 4.5209) <0.0001	<0.0001	
Non-White	196	155 (79.1)	41 (20.9)	0.1 (0.1, 0.1)	86	22 (25.6)	64 (74.4)	NE (8.2, NE)	5.2486 (3.3483, 8.2274) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.2863
Asia	147	113 (76.9)	34 (23.1)	0.1 (0.1, 0.1)	63	15 (23.8)	48 (76.2)	NE (11.7, NE)	5.1894 (3.0203, 8.9164) <0.0001	<0.0001	
North America	58	48 (82.8)	10 (17.2)	0.1 (0.1, 0.2)	28	9 (32.1)	19 (67.9)	6.0 (6.0, NE)	4.6129 (2.2451, 9.4780) <0.0001	<0.0001	
Europe + Israel	166	121 (72.9)	45 (27.1)	0.2 (0.1, 0.5)	81	28 (34.6)	53 (65.4)	NE (4.2, NE)	3.2174 (2.1273, 4.8662) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											
0	199	154 (77.4)	45 (22.6)	0.1 (0.1, 0.1)	95	28 (29.5)	67 (70.5)	NE (8.2, NE)	4.1483 (2.7666, 6.2200) <0.0001	<0.0001	0.7537
1	172	128 (74.4)	44 (25.6)	0.2 (0.1, 0.3)	77	24 (31.2)	53 (68.8)	NE (6.0, NE)	3.8116 (2.4575, 5.9120) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.8242
0	60	43 (71.7)	17 (28.3)	0.1 (0.1, 0.7)	31	10 (32.3)	21 (67.7)	NE (2.5, NE)	3.4966 (1.7492, 6.9896) 0.0004	0.0002	
1	107	83 (77.6)	24 (22.4)	0.1 (0.1, 0.2)	48	15 (31.3)	33 (68.8)	NE (8.2, NE)	4.3782 (2.5138, 7.6252) <0.0001	<0.0001	
2	114	83 (72.8)	31 (27.2)	0.1 (0.1, 0.5)	50	12 (24.0)	38 (76.0)	NE (6.0, NE)	4.6746 (2.5439, 8.5899) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 (81.1)	17 (18.9)	0.1 (0.1, 0.2)	43 (34.9)	28 (65.1)	11.7 (11.7, NE)	3.4482 (1.9723, 6.0286) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.8014
PD	173	127 (73.4)	46 (26.6)	0.2 (0.1, 0.3)	77	21 (27.3)	56 (72.7)	8.2 (6.0, NE)	4.1871 (2.6316, 6.6619)	<0.0001	
PR	48	37 (77.1)	11 (22.9)	0.1 (0.1, 0.3)	21	8 (38.1)	13 (61.9)	NE (0.3, NE)	3.1815 (1.4742, 6.8662)	0.0019	
SD	82	65 (79.3)	17 (20.7)	0.1 (0.1, 0.7)	54	18 (33.3)	36 (66.7)	NE (NE, NE)	3.7393 (2.2115, 6.3224)	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.5535
Yes	37	27 (73.0)	10 (27.0)	0.2 (0.1, 0.9)	13	5 (38.5)	8 (61.5)	NE (0.7, NE)	3.1148 (1.1917, 8.1410)	0.0147	
No	334	255 (76.3)	79 (23.7)	0.1 (0.1, 0.2)	159	47 (29.6)	112 (70.4)	NE (8.2, NE)	4.0942 (2.9937, 5.5994)	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.6652
Yes	24	14 (58.3)	10 (41.7)	1.1 (0.1, NE)	7	2 (28.6)	5 (71.4)	NE (0.1, NE)	2.7492 (0.6225, 12.1406) 0.1820	0.1594	
No	347	268 (77.2)	79 (22.8)	0.1 (0.1, 0.2)	165	50 (30.3)	115 (69.7)	NE (8.2, NE)	4.1116 (3.0339, 5.5720) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.4545
Normal Function	201	155 (77.1)	46 (22.9)	0.1 (0.1, 0.1)	80	22 (27.5)	58 (72.5)	NE (NE, NE)	4.6275 (2.9521, 7.2536) <0.0001	<0.0001	
Mild Impairment	123	93 (75.6)	30 (24.4)	0.1 (0.1, 0.2)	65	23 (35.4)	42 (64.6)	NE (2.5, NE)	3.2001 (2.0217, 5.0653) <0.0001	<0.0001	
Moderate Impairment	41	28 (68.3)	13 (31.7)	0.7 (0.2, 2.1)	23	7 (30.4)	16 (69.6)	NE (8.2, NE)	3.3541 (1.4562, 7.7257) 0.0045	0.0026	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.3340
Normal Function	170	133 (78.2)	37 (21.8)	0.1 (0.1, 0.1)	88	26 (29.5)	62 (70.5)	NE (11.7, NE)	4.5380 (2.9706, 6.9325) <0.0001	<0.0001	
Mild Impairment	194	143 (73.7)	51 (26.3)	0.2 (0.1, 0.3)	82	26 (31.7)	56 (68.3)	NE (8.2, NE)	3.3822 (2.2227, 5.1465) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.8902
Yes	331	252 (76.1)	79 (23.9)	0.1 (0.1, 0.2)	146	44 (30.1)	102 (69.9)	NE (8.2, NE)	4.0459 (2.9312, 5.5845) <0.0001	<0.0001	
No	40	30 (75.0)	10 (25.0)	0.1 (0.1, 0.8)	26	8 (30.8)	18 (69.2)	NE (0.7, NE)	3.7644 (1.7188, 8.2444) 0.0009	0.0004	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence  $\geq 10\%$  in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.7830
Positive	329	253 (76.9)	76 (23.1)	0.1 (0.1, 0.2)	152	46 (30.3)	106 (69.7)	NE (11.7, NE)	4.0525 (2.9540, 5.5593) <0.0001	<0.0001	
Negative	42	29 (69.0)	13 (31.0)	0.2 (0.1, 0.7)	20	6 (30.0)	14 (70.0)	NE (0.9, NE)	3.6022 (1.4876, 8.7228) 0.0045	0.0026	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.5814
Positive	331	254 (76.7)	77 (23.3)	0.1 (0.1, 0.2)	155	46 (29.7)	109 (70.3)	NE (11.7, NE)	4.1108 (2.9969, 5.6387)	<0.0001	
Negative	40	28 (70.0)	12 (30.0)	0.2 (0.1, 0.7)	17	6 (35.3)	11 (64.7)	NE (0.7, NE)	3.1976 (1.3165, 7.7661)	0.0071	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Vomiting

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.9599
HER2 IHC 1+	214	83 (38.8)	131 (61.2)	NE (10.6, NE)	100	13 (13.0)	87 (87.0)	NE (NE, NE)	3.2186 (1.7904, 5.7861) 0.0001	<0.0001	
HER2 IHC 2+/ISH Negative	157	67 (42.7)	90 (57.3)	NE (5.7, NE)	72	10 (13.9)	62 (86.1)	NE (NE, NE)	3.1418 (1.6143, 6.1145) 0.0008	0.0004	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Vomiting

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.0786
1	220	92 (41.8)	128 (58.2)	NE (9.3, NE)	94	9 (9.6)	85 (90.4)	NE (NE, NE)	4.7353 (2.3854, 9.4003) <0.0001	<0.0001	
>=2	150	57 (38.0)	93 (62.0)	NE (10.9, NE)	78	14 (17.9)	64 (82.1)	NE (6.8, NE)	2.1761 (1.2100, 3.9136) 0.0094	0.0079	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Gastrointestinal disorders; PT: Vomiting

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											
Yes	233	85 (36.5)	148 (63.5)	NE (10.6, NE)	112	14 (12.5)	98 (87.5)	NE (NE, NE)	2.8393 (1.6073, 5.0157) 0.0003	0.0002	0.1158
No	98	52 (53.1)	46 (46.9)	5.4 (1.4, NE)	43	4 (9.3)	39 (90.7)	NE (NE, NE)	7.1297 (2.5773, 19.7232) 0.0002	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Vomiting

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5104
<65	289	120 (41.5)	169 (58.5)	NE (9.5, NE)	126	16 (12.7)	110 (87.3)	NE (NE, NE)	3.4830 (2.0648, 5.8752) <0.0001	<0.0001	
>=65	82	30 (36.6)	52 (63.4)	NE (5.7, NE)	46	7 (15.2)	39 (84.8)	NE (NE, NE)	2.3928 (1.0476, 5.4653) 0.0384	0.0334	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Vomiting

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2771
<75	357	147 (41.2)	210 (58.8)	NE (10.3, NE)	163	23 (14.1)	140 (85.9)	NE (NE, NE)	3.0804 (1.9823, 4.7866) <0.0001	<0.0001	
>=75	14	3 (21.4)	11 (78.6)	NE (5.6, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9974	0.1697	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Vomiting

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.4686
White	175	72 (41.1)	103 (58.9)	NE (9.5, NE)	85	13 (15.3)	72 (84.7)	NE (NE, NE)	2.6613 (1.4689, 4.8216) 0.0012	0.0008	
Non-White	196	78 (39.8)	118 (60.2)	NE (9.3, NE)	86	10 (11.6)	76 (88.4)	NE (NE, NE)	3.7848 (1.9580, 7.3158) 0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Gastrointestinal disorders; PT: Vomiting

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.4645
Asia	147	57 (38.8)	90 (61.2)	NE (10.9, NE)	63	7 (11.1)	56 (88.9)	NE (NE, NE)	3.8404 (1.7502, 8.4267) 0.0008	0.0003	
North America	58	28 (48.3)	30 (51.7)	10.6 (0.9, NE)	28	3 (10.7)	25 (89.3)	NE (6.0, NE)	4.8671 (1.4704, 16.1108) 0.0096	0.0042	
Europe + Israel	166	65 (39.2)	101 (60.8)	NE (9.5, NE)	81	13 (16.0)	68 (84.0)	NE (NE, NE)	2.4214 (1.3309, 4.4054) 0.0038	0.0028	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Gastrointestinal disorders; PT: Vomiting

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.1028
0	199	74 (37.2)	125 (62.8)	NE (12.1, NE)	95	7 (7.4)	88 (92.6)	NE (NE, NE)	5.0716 (2.3332, 11.0240) <0.0001	<0.0001	
1	172	76 (44.2)	96 (55.8)	10.9 (5.0, NE)	77	16 (20.8)	61 (79.2)	NE (6.8, NE)	2.3637 (1.3758, 4.0609) 0.0018	0.0014	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Gastrointestinal disorders; PT: Vomiting

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.2505
0	60	20 (33.3)	40 (66.7)	NE (5.1, NE)	31	6 (19.4)	25 (80.6)	NE (NE, NE)	1.6797 (0.6740, 4.1858) 0.2656	0.2597	
1	107	42 (39.3)	65 (60.7)	NE (9.3, NE)	48	8 (16.7)	40 (83.3)	NE (NE, NE)	2.6555 (1.2450, 5.6642) 0.0115	0.0089	
2	114	60 (52.6)	54 (47.4)	5.4 (2.1, NE)	50	5 (10.0)	45 (90.0)	NE (6.0, NE)	5.7729 (2.3135, 14.4053) 0.0002	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	28 (31.1)	62 (68.9)	43	4 (9.3)	39 (90.7)	NE (12.1, NE)	3.2188 (1.1227, 9.2282) 0.0296	0.0215

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.3455
PD	173	72 (41.6)	101 (58.4)	NE (5.6, NE)	77	10 (13.0)	67 (87.0)	NE (NE, NE)	3.3876 (1.7460, 6.5729) 0.0003	0.0001	
PR	48	14 (29.2)	34 (70.8)	NE (NE, NE)	21	4 (19.0)	17 (81.0)	NE (NE, NE)	1.4401 (0.4726, 4.3887) 0.5212	0.5196	
SD	82	36 (43.9)	46 (56.1)	12.1 (4.3, NE)	54	7 (13.0)	47 (87.0)	NE (NE, NE)	3.6404 (1.6162, 8.2000) 0.0018	0.0009	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.2589
Yes	37	13 (35.1)	24 (64.9)	NE (1.5, NE)	13	3 (23.1)	10 (76.9)	6.8 (0.8, NE)	1.5526 (0.4409, 5.4678)	0.4895	
No	334	137 (41.0)	197 (59.0)	NE (10.4, NE)	159	20 (12.6)	139 (87.4)	NE (NE, NE)	3.4402 (2.1494, 5.5061)	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.4391
Yes	24	10 (41.7)	14 (58.3)	NE (0.8, NE)	7	2 (28.6)	5 (71.4)	6.8 (0.8, NE)	1.7593 (0.3843, 8.0541) 0.4667	0.4568	
No	347	140 (40.3)	207 (59.7)	NE (10.4, NE)	165	21 (12.7)	144 (87.3)	NE (NE, NE)	3.3112 (2.0906, 5.2443) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Gastrointestinal disorders; PT: Vomiting

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.5820
Normal Function	201	87 (43.3)	114 (56.7)	12.1 (8.3, NE)	80	10 (12.5)	70 (87.5)	NE (NE, NE)	3.7839 (1.9638, 7.2909) 0.0001	<0.0001	
Mild Impairment	123	40 (32.5)	83 (67.5)	NE (NE, NE)	65	9 (13.8)	56 (86.2)	NE (NE, NE)	2.3122 (1.1186, 4.7796) 0.0237	0.0201	
Moderate Impairment	41	19 (46.3)	22 (53.7)	10.9 (1.0, NE)	23	4 (17.4)	19 (82.6)	NE (6.8, NE)	2.9139 (0.9906, 8.5712) 0.0520	0.0419	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Vomiting

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.5707
Normal Function	170	77 (45.3)	93 (54.7)	12.1 (5.7, NE)	88	15 (17.0)	73 (83.0)	NE (NE, NE)	2.8846 (1.6565, 5.0229) 0.0002	<0.0001	
Mild Impairment	194	69 (35.6)	125 (64.4)	NE (10.4, NE)	82	8 (9.8)	74 (90.2)	NE (NE, NE)	3.6781 (1.7649, 7.6651) 0.0005	0.0002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Vomiting

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.0758
Yes	331	131 (39.6)	200 (60.4)	NE (12.1, NE)	146	16 (11.0)	130 (89.0)	NE (NE, NE)	3.9479 (2.3473, 6.6399) <0.0001	<0.0001	
No	40	19 (47.5)	21 (52.5)	10.4 (1.7, NE)	26	7 (26.9)	19 (73.1)	NE (NE, NE)	1.4200 (0.5872, 3.4343) 0.4364	0.4355	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Vomiting

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.1061
Positive	329	135 (41.0)	194 (59.0)	NE (10.4, NE)	152	18 (11.8)	134 (88.2)	NE (NE, NE)	3.6870 (2.2521, 6.0362) <0.0001	<0.0001	
Negative	42	15 (35.7)	27 (64.3)	NE (3.4, NE)	20	5 (25.0)	15 (75.0)	NE (0.9, NE)	1.3684 (0.4954, 3.7796) 0.5451	0.5407	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Vomiting

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.0255
Positive	331	138 (41.7)	193 (58.3)	NE (10.4, NE)	155	18 (11.6)	137 (88.4)	NE (NE, NE)	3.8448 (2.3501, 6.2901)	<0.0001	
Negative	40	12 (30.0)	28 (70.0)	NE (5.1, NE)	17	5 (29.4)	12 (70.6)	NE (0.7, NE)	0.9018 (0.3152, 2.5796)	0.8471	0.8496

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Constipation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.4002
HER2 IHC 1+	214	68 (31.8)	146 (68.2)	NE (17.3, NE)	100	23 (23.0)	77 (77.0)	NE (6.5, NE)	1.1934 (0.7407, 1.9229) 0.4676	0.4704	
HER2 IHC 2+/ISH Negative	157	58 (36.9)	99 (63.1)	NE (11.2, NE)	72	15 (20.8)	57 (79.2)	NE (7.6, NE)	1.6323 (0.9214, 2.8917) 0.0931	0.0903	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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SOC: Gastrointestinal disorders; PT: Constipation

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting									0.8356
1	220 (33.6)	74 (33.6)	146 (66.4) (17.3, NE)	94 (23.4)	22 (23.4)	72 (76.6) (7.6, NE)	1.2954 (0.8017, 2.0933) 0.2904	0.2927	
>=2	150 (34.0)	51 (34.0)	99 (66.0) (14.6, NE)	78 (20.5)	16 (20.5)	62 (79.5) (NE, NE)	1.4795 (0.8407, 2.6035) 0.1744	0.1715	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Constipation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.9287
Yes	233	81 (34.8)	152 (65.2)	NE (16.5, NE)	112	26 (23.2)	86 (76.8)	10.9 (6.5, NE)	1.3488 (0.8636, 2.1069) 0.1884	0.1890	
No	98	31 (31.6)	67 (68.4)	NE (14.6, NE)	43	9 (20.9)	34 (79.1)	NE (NE, NE)	1.2982 (0.6155, 2.7382) 0.4931	0.4935	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Constipation

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Age											
<65	289	97 (33.6)	192 (66.4)	NE (17.3, NE)	126	26 (20.6)	100 (79.4)	NE (7.6, NE)	1.4309 (0.9247, 2.2142) 0.1077	0.1067	0.8001
>=65	82	29 (35.4)	53 (64.6)	NE (11.5, NE)	46	12 (26.1)	34 (73.9)	NE (5.3, NE)	1.2888 (0.6553, 2.5350) 0.4622	0.4657	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Constipation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6456
<75	357	123 (34.5)	234 (65.5)	NE (17.3, NE)	163	36 (22.1)	127 (77.9)	NE (10.9, NE)	1.3865 (0.9532, 2.0166) 0.0874	0.0874	
>=75	14	3 (21.4)	11 (78.6)	NE (4.1, NE)	9	2 (22.2)	7 (77.8)	NE (0.1, NE)	0.8521 (0.1419, 5.1168) 0.8611	0.8609	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Constipation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.0808
White	175	50 (28.6)	125 (71.4)	NE (17.3, NE)	85	21 (24.7)	64 (75.3)	NE (6.5, NE)	0.9395 (0.5602, 1.5758) 0.8131	0.8105	
Non-White	196	76 (38.8)	120 (61.2)	NE (11.2, NE)	86	17 (19.8)	69 (80.2)	NE (10.9, NE)	1.9125 (1.1279, 3.2428) 0.0161	0.0144	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Constipation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.0475
Asia	147	57 (38.8)	90 (61.2)	NE (11.2, NE)	63	10 (15.9)	53 (84.1)	NE (10.9, NE)	2.3449 (1.1934, 4.6075) 0.0134	0.0110	
North America	58	25 (43.1)	33 (56.9)	11.5 (3.7, NE)	28	7 (25.0)	21 (75.0)	7.6 (5.7, NE)	1.6353 (0.7003, 3.8185) 0.2557	0.2529	
Europe + Israel	166	44 (26.5)	122 (73.5)	NE (NE, NE)	81	21 (25.9)	60 (74.1)	NE (6.5, NE)	0.8437 (0.4990, 1.4263) 0.5257	0.5242	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Constipation

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	199	70 (35.2)	129 (64.8)	NE (16.5, NE)	95	17 (17.9)	78 (82.1)	NE (10.9, NE)	1.7410 (1.0215, 2.9674) 0.0415	0.0394	0.1952
1	172	56 (32.6)	116 (67.4)	NE (17.3, NE)	77	21 (27.3)	56 (72.7)	NE (6.5, NE)	1.0855 (0.6541, 1.8013) 0.7509	0.7625	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Constipation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.0158
0	60	20 (33.3)	40 (66.7)	NE (14.6, NE)	31	7 (22.6)	24 (77.4)	NE (5.3, NE)	1.3435 (0.5661, 3.1881) 0.5031	0.5064	
1	107	28 (26.2)	79 (73.8)	NE (16.5, NE)	48	14 (29.2)	34 (70.8)	NE (6.5, NE)	0.8492 (0.4457, 1.6182) 0.6193	0.6114	
2	114	38 (33.3)	76 (66.7)	NE (17.3, NE)	50	13 (26.0)	37 (74.0)	NE (5.7, NE)	1.0676 (0.5650, 2.0173) 0.8402	0.8377	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Constipation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	40 (44.4)	50 (55.6)	10.8 (4.8, NE)	43	4 (9.3)	39 (90.7)	NE (10.9, NE)	4.4733 (1.5923, 12.5673) 0.0045	0.0019	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Constipation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.6789
PD	173	51 (29.5)	122 (70.5)	NE (NE, NE)	77	17 (22.1)	60 (77.9)	NE (7.6, NE)	1.1422 (0.6552, 1.9912) 0.6392	0.6469	
PR	48	17 (35.4)	31 (64.6)	17.3 (10.5, NE)	21	3 (14.3)	18 (85.7)	NE (NE, NE)	1.8745 (0.5420, 6.4831) 0.3209	0.3132	
SD	82	28 (34.1)	54 (65.9)	NE (14.6, NE)	54	14 (25.9)	40 (74.1)	NE (6.5, NE)	1.1857 (0.6196, 2.2690) 0.6069	0.6107	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Constipation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.5378
Yes	37	18 (48.6)	19 (51.4)	4.2 (0.8, NE)	13	3 (23.1)	10 (76.9)	NE (0.8, NE)	1.9022 (0.5570, 6.4962) 0.3048	0.2954	
No	334	108 (32.3)	226 (67.7)	NE (NE, NE)	159	35 (22.0)	124 (78.0)	NE (10.9, NE)	1.3022 (0.8864, 1.9130) 0.1784	0.1805	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Constipation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.9566
Yes	24	10 (41.7)	14 (58.3)	NE (0.7, NE)	7	2 (28.6)	5 (71.4)	NE (0.1, NE)	1.3998 (0.3021, 6.4863) 0.6673	0.6714	
No	347	116 (33.4)	231 (66.6)	NE (NE, NE)	165	36 (21.8)	129 (78.2)	NE (10.9, NE)	1.3570 (0.9308, 1.9785) 0.1125	0.1129	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Constipation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.7745
Normal Function	201	68 (33.8)	133 (66.2)	NE (14.6, NE)	80	20 (25.0)	60 (75.0)	NE (10.9, NE)	1.1728 (0.7088, 1.9405) 0.5351	0.5392	
Mild Impairment	123	45 (36.6)	78 (63.4)	NE (11.2, NE)	65	14 (21.5)	51 (78.5)	NE (6.5, NE)	1.5717 (0.8591, 2.8754) 0.1423	0.1398	
Moderate Impairment	41	11 (26.8)	30 (73.2)	NE (16.5, NE)	23	4 (17.4)	19 (82.6)	NE (NE, NE)	1.4220 (0.4504, 4.4898) 0.5484	0.5455	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Constipation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.3502
Normal Function	170	64 (37.6)	106 (62.4)	NE (14.6, NE)	88	19 (21.6)	69 (78.4)	NE (10.9, NE)	1.5729 (0.9383, 2.6366) 0.0857	0.0842	
Mild Impairment	194	61 (31.4)	133 (68.6)	NE (NE, NE)	82	19 (23.2)	63 (76.8)	NE (6.5, NE)	1.2169 (0.7247, 2.0433) 0.4578	0.4563	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Constipation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.7607
Yes	331	111 (33.5)	220 (66.5)	NE (17.3, NE)	146	33 (22.6)	113 (77.4)	NE (10.9, NE)	1.3488 (0.9122, 1.9946) 0.1338	0.1334	
No	40	15 (37.5)	25 (62.5)	NE (5.7, NE)	26	5 (19.2)	21 (80.8)	NE (2.8, NE)	1.4786 (0.5244, 4.1696) 0.4596	0.4588	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Constipation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.9543
Positive	329	111 (33.7)	218 (66.3)	NE (17.3, NE)	152	33 (21.7)	119 (78.3)	NE (10.9, NE)	1.3763 (0.9301, 2.0363) 0.1101	0.1100	
Negative	42	15 (35.7)	27 (64.3)	NE (3.5, NE)	20	5 (25.0)	15 (75.0)	NE (2.0, NE)	1.3820 (0.5006, 3.8149) 0.5323	0.5375	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Constipation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.4995
Positive	331	111 (33.5)	220 (66.5)	NE (17.3, NE)	155	35 (22.6)	120 (77.4)	NE (10.9, NE)	1.3108 (0.8936, 1.9229)	0.1662	0.1669
Negative	40	15 (37.5)	25 (62.5)	NE (3.5, NE)	17	3 (17.6)	14 (82.4)	NE (NE, NE)	2.1181 (0.6109, 7.3437)	0.2367	0.2286

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Diarrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0401
HER2 IHC 1+	214	57 (26.6)	157 (73.4)	NE (NE, NE)	100	28 (28.0)	72 (72.0)	NE (7.1, NE)	0.7888 (0.4989, 1.2471) 0.3101	0.3092	
HER2 IHC 2+/ISH Negative	157	43 (27.4)	114 (72.6)	NE (NE, NE)	72	10 (13.9)	62 (86.1)	NE (NE, NE)	1.8292 (0.9157, 3.6539) 0.0872	0.0828	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Diarrhoea

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting									0.9025
1	220	59 (26.8)	161 (73.2) NE (NE, NE)	94	21 (22.3)	73 (77.7) NE (NE, NE)	1.0858 (0.6581, 1.7915) 0.7472	0.7488	
>=2	150	41 (27.3)	109 (72.7) NE (13.9, NE)	78	17 (21.8)	61 (78.2) NE (NE, NE)	1.0596 (0.5984, 1.8762) 0.8426	0.8458	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Diarrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.9946
Yes	233	72 (30.9)	161 (69.1)	NE (NE, NE)	112	26 (23.2)	86 (76.8)	NE (NE, NE)	1.1554 (0.7349, 1.8165) 0.5315	0.5311	
No	98	18 (18.4)	80 (81.6)	NE (NE, NE)	43	6 (14.0)	37 (86.0)	NE (NE, NE)	1.1284 (0.4452, 2.8601) 0.7990	0.8010	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Diarrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4563
<65	289	76 (26.3)	213 (73.7)	NE (NE, NE)	126	24 (19.0)	102 (81.0)	NE (NE, NE)	1.1963 (0.7532, 1.9000) 0.4477	0.4479	
>=65	82	24 (29.3)	58 (70.7)	NE (13.9, NE)	46	14 (30.4)	32 (69.6)	NE (7.1, NE)	0.8860 (0.4562, 1.7209) 0.7208	0.7146	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Diarrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8304
<75	357	96 (26.9)	261 (73.1)	NE (NE, NE)	163	35 (21.5)	128 (78.5)	NE (NE, NE)	1.0839 (0.7336, 1.6014) 0.6859	0.6882	
>=75	14	4 (28.6)	10 (71.4)	NE (0.3, NE)	9	3 (33.3)	6 (66.7)	NE (0.4, NE)	0.9293 (0.2076, 4.1608) 0.9237	0.9236	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Diarrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.4413
White	175	59 (33.7)	116 (66.3)	NE (NE, NE)	85	21 (24.7)	64 (75.3)	NE (NE, NE)	1.2516 (0.7584, 2.0657) 0.3799	0.3830	
Non-White	196	41 (20.9)	155 (79.1)	NE (NE, NE)	86	17 (19.8)	69 (80.2)	NE (NE, NE)	0.8847 (0.4993, 1.5674) 0.6745	0.6725	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Diarrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.0631
Asia	147	24 (16.3)	123 (83.7)	NE (NE, NE)	63	14 (22.2)	49 (77.8)	NE (NE, NE)	0.5876 (0.3014, 1.1457) 0.1186	0.1143	
North America	58	23 (39.7)	35 (60.3)	NE (1.5, NE)	28	5 (17.9)	23 (82.1)	NE (NE, NE)	2.2558 (0.8534, 5.9625) 0.1009	0.0941	
Europe + Israel	166	53 (31.9)	113 (68.1)	NE (13.9, NE)	81	19 (23.5)	62 (76.5)	NE (7.1, NE)	1.2371 (0.7302, 2.0961) 0.4289	0.4303	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Diarrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.8327
0	199	50 (25.1)	149 (74.9)	NE (NE, NE)	95	20 (21.1)	75 (78.9)	NE (NE, NE)	1.0785 (0.6398, 1.8181) 0.7765	0.7820	
1	172	50 (29.1)	122 (70.9)	NE (13.9, NE)	77	18 (23.4)	59 (76.6)	NE (NE, NE)	1.0632 (0.6170, 1.8320) 0.8253	0.8222	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Diarrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.2094
0	60	14 (23.3)	46 (76.7)	NE (NE, NE)	31	7 (22.6)	24 (77.4)	NE (4.9, NE)	0.8952 (0.3582, 2.2372) 0.8127	0.8080	
1	107	20 (18.7)	87 (81.3)	NE (NE, NE)	48	11 (22.9)	37 (77.1)	NE (NE, NE)	0.6767 (0.3231, 1.4173) 0.3005	0.2986	
2	114	42 (36.8)	72 (63.2)	NE (13.9, NE)	50	9 (18.0)	41 (82.0)	NE (NE, NE)	1.9865 (0.9630, 4.0975) 0.0632	0.0587	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Diarrhoea

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	24 (26.7)	66 (73.3)	43	11 (25.6)	32 (74.4)	NE (NE, NE)	0.8739 (0.4243, 1.7998) 0.7146	0.7100

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Diarrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.0578
PD	173	52 (30.1)	121 (69.9)	NE (13.9, NE)	77	11 (14.3)	66 (85.7)	NE (NE, NE)	1.8950 (0.9836, 3.6512) 0.0561	0.0526	
PR	48	8 (16.7)	40 (83.3)	NE (NE, NE)	21	5 (23.8)	16 (76.2)	NE (5.0, NE)	0.5375 (0.1723, 1.6767) 0.2849	0.2782	
SD	82	25 (30.5)	57 (69.5)	NE (10.4, NE)	54	17 (31.5)	37 (68.5)	NE (NE, NE)	0.8292 (0.4457, 1.5428) 0.5544	0.5543	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Diarrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.3693
Yes	37	8 (21.6)	29 (78.4)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	2.4222 (0.3004, 19.5332) 0.4062	0.3859	
No	334	92 (27.5)	242 (72.5)	NE (NE, NE)	159	37 (23.3)	122 (76.7)	NE (NE, NE)	1.0394 (0.7074, 1.5270) 0.8441	0.8461	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Diarrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.7823
Yes	24	5 (20.8)	19 (79.2)	NE (9.5, NE)	7	1 (14.3)	6 (85.7)	NE (0.1, NE)	1.2574 (0.1451, 10.9002) 0.8353	0.8236	
No	347	95 (27.4)	252 (72.6)	NE (NE, NE)	165	37 (22.4)	128 (77.6)	NE (NE, NE)	1.0647 (0.7260, 1.5616) 0.7482	0.7510	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Diarrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.8478
Normal Function	201	52 (25.9)	149 (74.1)	NE (NE, NE)	80	16 (20.0)	64 (80.0)	NE (NE, NE)	1.1176 (0.6351, 1.9665) 0.6998	0.7031	
Mild Impairment	123	36 (29.3)	87 (70.7)	NE (NE, NE)	65	14 (21.5)	51 (78.5)	NE (NE, NE)	1.2128 (0.6494, 2.2651) 0.5449	0.5449	
Moderate Impairment	41	12 (29.3)	29 (70.7)	NE (13.9, NE)	23	7 (30.4)	16 (69.6)	NE (7.1, NE)	0.8963 (0.3527, 2.2776) 0.8180	0.8193	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Diarrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.7760
Normal Function	170	54 (31.8)	116 (68.2)	NE (NE, NE)	88	22 (25.0)	66 (75.0)	NE (NE, NE)	1.1197 (0.6794, 1.8454) 0.6574	0.6591	
Mild Impairment	194	44 (22.7)	150 (77.3)	NE (NE, NE)	82	16 (19.5)	66 (80.5)	NE (7.1, NE)	1.0058 (0.5646, 1.7918) 0.9844	0.9883	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Diarrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.7610
Yes	331	89 (26.9)	242 (73.1)	NE (NE, NE)	146	32 (21.9)	114 (78.1)	NE (NE, NE)	1.0978 (0.7310, 1.6488) 0.6530	0.6561	
No	40	11 (27.5)	29 (72.5)	NE (NE, NE)	26	6 (23.1)	20 (76.9)	NE (5.0, NE)	0.9300 (0.3400, 2.5436) 0.8876	0.8881	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Diarrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.3425
Positive	329	89 (27.1)	240 (72.9)	NE (NE, NE)	152	31 (20.4)	121 (79.6)	NE (NE, NE)	1.1562 (0.7660, 1.7452) 0.4895	0.4894	
Negative	42	11 (26.2)	31 (73.8)	NE (NE, NE)	20	7 (35.0)	13 (65.0)	5.0 (2.8, NE)	0.7116 (0.2740, 1.8476) 0.4845	0.4735	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Diarrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.3049
Positive	331	90 (27.2)	241 (72.8)	NE (NE, NE)	155	32 (20.6)	123 (79.4)	NE (NE, NE)	1.1558 (0.7700, 1.7349)	0.4849	0.4854
Negative	40	10 (25.0)	30 (75.0)	NE (NE, NE)	17	6 (35.3)	11 (64.7)	4.9 (2.8, NE)	0.5725 (0.2000, 1.6386)	0.2986	0.2863

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.6750
HER2 IHC 1+	214	24 (11.2)	190 (88.8)	NE (NE, NE)	100	11 (11.0)	89 (89.0)	NE (11.3, NE)	0.7383 (0.3574, 1.5251) 0.4124	0.4115	
HER2 IHC 2+/ISH Negative	157	17 (10.8)	140 (89.2)	NE (NE, NE)	72	6 (8.3)	66 (91.7)	NE (NE, NE)	0.9931 (0.3882, 2.5405) 0.9885	0.9891	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting									0.7885
1	220	24 (10.9)	196 (89.1)	94	10 (10.6)	84 (89.4)	0.7887 (0.3735, 1.6655) 0.5337	0.5334	
>=2	150	17 (11.3)	133 (88.7)	78	7 (9.0)	71 (91.0)	0.8503 (0.3470, 2.0839) 0.7230	0.7231	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.5169
Yes	233	25 (10.7)	208 (89.3)	NE (NE, NE)	112	13 (11.6)	99 (88.4)	NE (NE, NE)	0.7015 (0.3552, 1.3853) 0.3072	0.3055	
No	98	12 (12.2)	86 (87.8)	NE (NE, NE)	43	4 (9.3)	39 (90.7)	NE (11.3, NE)	0.9036 (0.2880, 2.8351) 0.8620	0.8620	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6472
<65	289	28 (9.7)	261 (90.3)	NE (NE, NE)	126	9 (7.1)	117 (92.9)	NE (11.3, NE)	0.9957 (0.4650, 2.1322) 0.9911	0.9911	
>=65	82	13 (15.9)	69 (84.1)	NE (NE, NE)	46	8 (17.4)	38 (82.6)	NE (NE, NE)	0.7056 (0.2895, 1.7197) 0.4429	0.4439	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6956
<75	357	39 (10.9)	318 (89.1)	NE (NE, NE)	163	16 (9.8)	147 (90.2)	NE (NE, NE)	0.7923 (0.4381, 1.4330) 0.4413	0.4406	
>=75	14	2 (14.3)	12 (85.7)	NE (3.8, NE)	9	1 (11.1)	8 (88.9)	NE (0.6, NE)	1.3370 (0.1211, 14.7574) 0.8126	0.8120	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.9911
White	175	14 (8.0)	161 (92.0)	NE (NE, NE)	85	6 (7.1)	79 (92.9)	NE (NE, NE)	0.8993 (0.3418, 2.3661) 0.8297	0.8299	
Non-White	196	27 (13.8)	169 (86.2)	NE (NE, NE)	86	11 (12.8)	75 (87.2)	NE (11.3, NE)	0.7734 (0.3798, 1.5747) 0.4787	0.4778	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.5530
Asia	147	23 (15.6)	124 (84.4)	NE (NE, NE)	63	7 (11.1)	56 (88.9)	NE (NE, NE)	1.0000 (0.4251, 2.3523) 1.0000	0.9993	
North America	58	6 (10.3)	52 (89.7)	NE (NE, NE)	28	2 (7.1)	26 (92.9)	NE (NE, NE)	1.1876 (0.2385, 5.9140) 0.8338	0.8336	
Europe + Israel	166	12 (7.2)	154 (92.8)	NE (NE, NE)	81	8 (9.9)	73 (90.1)	NE (11.3, NE)	0.5416 (0.2168, 1.3530) 0.1892	0.1828	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.6149
0	199	19 (9.5)	180 (90.5)	NE (NE, NE)	95	9 (9.5)	86 (90.5)	NE (NE, NE)	0.7337 (0.3286, 1.6384) 0.4500	0.4493	
1	172	22 (12.8)	150 (87.2)	NE (NE, NE)	77	8 (10.4)	69 (89.6)	NE (11.3, NE)	0.9036 (0.3954, 2.0647) 0.8099	0.8100	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.6289
0	60	5 (8.3)	55 (91.7)	NE (NE, NE)	31	3 (9.7)	28 (90.3)	NE (NE, NE)	0.5720 (0.1313, 2.4920) 0.4569	0.4518	
1	107	12 (11.2)	95 (88.8)	NE (NE, NE)	48	3 (6.3)	45 (93.8)	NE (NE, NE)	1.6017 (0.4497, 5.7052) 0.4674	0.4642	
2	114	10 (8.8)	104 (91.2)	NE (NE, NE)	50	5 (10.0)	45 (90.0)	11.3 (11.3, NE)	0.6217 (0.2088, 1.8507) 0.3931	0.3895	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 (15.6)	76 (84.4)	NE (NE, NE)	43 (14.0)	37 (86.0)	NE (NE, NE)	0.6871 (0.2572, 1.8353) 0.4540	0.4534	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.9415
PD	173	15 (8.7)	158 (91.3)	NE (NE, NE)	77	6 (7.8)	71 (92.2)	11.3 (11.3, NE)	0.8044 (0.3077, 2.1029)	0.6554	
PR	48	5 (10.4)	43 (89.6)	NE (NE, NE)	21	2 (9.5)	19 (90.5)	NE (NE, NE)	0.6571 (0.0984, 3.2030)	0.5106	
SD	82	13 (15.9)	69 (84.1)	NE (NE, NE)	54	7 (13.0)	47 (87.0)	NE (NE, NE)	0.9177 (0.3614, 2.3304)	0.8600	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.6800
Yes	37	2 (5.4)	35 (94.6)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	0.4325 (0.0365, 5.1305) 0.5066	0.4951	
No	334	39 (11.7)	295 (88.3)	NE (NE, NE)	159	16 (10.1)	143 (89.9)	NE (NE, NE)	0.8542 (0.4732, 1.5419) 0.6009	0.6012	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.4002
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	1 (14.3)	6 (85.7)	NE (0.7, NE)	0.2887 (0.0181, 4.6154) 0.3797	0.3492	
No	347	40 (11.5)	307 (88.5)	NE (NE, NE)	165	16 (9.7)	149 (90.3)	NE (NE, NE)	0.8565 (0.4752, 1.5437) 0.6062	0.6065	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.5535
Normal Function	201	19 (9.5)	182 (90.5)	NE (NE, NE)	80	7 (8.8)	73 (91.3)	NE (NE, NE)	0.8189 (0.3387, 1.9803) 0.6575	0.6572	
Mild Impairment	123	15 (12.2)	108 (87.8)	NE (NE, NE)	65	7 (10.8)	58 (89.2)	NE (11.3, NE)	0.7902 (0.3171, 1.9692) 0.6133	0.6128	
Moderate Impairment	41	7 (17.1)	34 (82.9)	NE (NE, NE)	23	2 (8.7)	21 (91.3)	NE (NE, NE)	1.8041 (0.3744, 8.6944) 0.4621	0.4556	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.0771
Normal Function	170	20 (11.8)	150 (88.2)	NE (NE, NE)	88	5 (5.7)	83 (94.3)	NE (NE, NE)	1.3612 (0.5032, 3.6822) 0.5436	0.5417	
Mild Impairment	194	21 (10.8)	173 (89.2)	NE (NE, NE)	82	12 (14.6)	70 (85.4)	NE (11.3, NE)	0.5720 (0.2793, 1.1716) 0.1268	0.1222	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.5560
Yes	331	35 (10.6)	296 (89.4)	NE (NE, NE)	146	15 (10.3)	131 (89.7)	NE (NE, NE)	0.7592 (0.4113, 1.4016) 0.3785	0.3776	
No	40	6 (15.0)	34 (85.0)	NE (NE, NE)	26	2 (7.7)	24 (92.3)	NE (NE, NE)	1.4654 (0.2838, 7.5662) 0.6482	0.6462	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.6211
Positive	329	37 (11.2)	292 (88.8)	NE (NE, NE)	152	16 (10.5)	136 (89.5)	NE (NE, NE)	0.7807 (0.4306, 1.4154) 0.4147	0.4144	
Negative	42	4 (9.5)	38 (90.5)	NE (NE, NE)	20	1 (5.0)	19 (95.0)	NE (NE, NE)	1.5626 (0.1699, 14.3740) 0.6934	0.6911	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.1071
Positive	331	37 (11.2)	294 (88.8)	NE (NE, NE)	155	17 (11.0)	138 (89.0)	NE (NE, NE)	0.7459 (0.4163, 1.3362)	0.3233	
Negative	40	4 (10.0)	36 (90.0)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	0.3243 (NE, NE)	0.2387	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.6573
HER2 IHC 1+	214	144 (67.3)	70 (32.7)	2.8 (1.8, 4.1)	100	67 (67.0)	33 (33.0)	0.5 (0.5, 1.4)	0.6962 (0.5193, 0.9333) 0.0155	0.0154	
HER2 IHC 2+/ISH Negative	157	107 (68.2)	50 (31.8)	3.4 (2.1, 4.2)	72	47 (65.3)	25 (34.7)	0.7 (0.5, 3.5)	0.7575 (0.5351, 1.0722) 0.1172	0.1226	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.5026
1	220	143 (65.0)	77 (35.0)	3.4 (2.3, 4.2)	94	57 (60.6)	37 (39.4)	0.9 (0.5, 3.9)	0.7949 (0.5833, 1.0835) 0.1464	0.1537	
>=2	150	108 (72.0)	42 (28.0)	2.7 (1.4, 3.5)	78	57 (73.1)	21 (26.9)	0.5 (0.4, 0.9)	0.6627 (0.4783, 0.9183) 0.0134	0.0130	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Prior CDK4/6											
Yes	233	147 (63.1)	86 (36.9)	3.7 (2.7, 4.2)	112	70 (62.5)	42 (37.5)	0.9 (0.5, 3.3)	0.7093 (0.5315, 0.9467) 0.0197	0.0199	0.6851
No	98	75 (76.5)	23 (23.5)	1.4 (0.6, 3.5)	43	32 (74.4)	11 (25.6)	0.5 (0.3, 0.7)	0.7704 (0.5080, 1.1682) 0.2194	0.2261	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9300
<65	289	194 (67.1)	95 (32.9)	2.8 (2.1, 4.1)	126	80 (63.5)	46 (36.5)	0.7 (0.5, 2.1)	0.7433 (0.5711, 0.9675) 0.0274	0.0294	
>=65	82	57 (69.5)	25 (30.5)	3.4 (1.2, 5.4)	46	34 (73.9)	12 (26.1)	0.7 (0.3, 3.5)	0.7044 (0.4592, 1.0807) 0.1086	0.1125	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7820
<75	357	240 (67.2)	117 (32.8)	2.8 (2.1, 4.1)	163	107 (65.6)	56 (34.4)	0.7 (0.5, 1.4)	0.7348 (0.5837, 0.9251) 0.0087	0.0093	
>=75	14	11 (78.6)	3 (21.4)	3.0 (0.7, 4.2)	9	7 (77.8)	2 (22.2)	0.7 (0.2, NE)	0.4613 (0.1657, 1.2844) 0.1386	0.1293	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.1095
White	175	110 (62.9)	65 (37.1)	4.2 (3.0, 6.2)	85	46 (54.1)	39 (45.9)	3.5 (0.7, 7.2)	0.8313 (0.5862, 1.1788) 0.2998	0.3301	
Non-White	196	141 (71.9)	55 (28.1)	1.4 (0.7, 2.8)	86	68 (79.1)	18 (20.9)	0.5 (0.3, 0.5)	0.6054 (0.4518, 0.8112) 0.0008	0.0006	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.0048
Asia	147	114 (77.6)	33 (22.4)	1.3 (0.5, 2.2)	63	56 (88.9)	7 (11.1)	0.3 (0.3, 0.5)	0.4590 (0.3302, 0.6380) <0.0001	<0.0001	
North America	58	38 (65.5)	20 (34.5)	4.0 (2.1, 5.5)	28	19 (67.9)	9 (32.1)	0.7 (0.3, 3.9)	0.6442 (0.3699, 1.1219) 0.1203	0.1311	
Europe + Israel	166	99 (59.6)	67 (40.4)	4.2 (3.3, 6.4)	81	39 (48.1)	42 (51.9)	5.5 (2.1, 7.2)	0.9762 (0.6703, 1.4216) 0.9000	0.9212	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
ECOG PS											
0	199	138 (69.3)	61 (30.7)	3.5 (1.4, 4.2)	95	58 (61.1)	37 (38.9)	0.9 (0.5, 3.9)	0.8433 (0.6191, 1.1489) 0.2801	0.3016	0.1551
1	172	113 (65.7)	59 (34.3)	2.8 (2.1, 3.5)	77	56 (72.7)	21 (27.3)	0.5 (0.5, 0.9)	0.5914 (0.4266, 0.8200) 0.0016	0.0015	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.2800
0	60	39 (65.0)	21 (35.0)	2.8 (2.0, 6.3)	31	23 (74.2)	8 (25.8)	0.7 (0.3, 2.1)	0.5121 (0.2998, 0.8748) 0.0143	0.0129	
1	107	71 (66.4)	36 (33.6)	3.7 (1.5, 4.8)	48	31 (64.6)	17 (35.4)	0.7 (0.3, 6.9)	0.7769 (0.5084, 1.1874) 0.2435	0.2421	
2	114	79 (69.3)	35 (30.7)	2.1 (0.7, 3.5)	50	29 (58.0)	21 (42.0)	0.9 (0.5, NE)	0.9982 (0.6501, 1.5329) 0.9936	0.9843	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	62 (68.9)	28 (31.1)	3.5 (2.1, 5.6)	43	31 (72.1)	12 (27.9)	0.5 (0.3, 1.4)	0.5617 (0.3601, 0.8759) 0.0110	0.0108	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.4930
PD	173	112 (64.7)	61 (35.3)	3.3 (2.3, 4.3)	77	50 (64.9)	27 (35.1)	0.9 (0.5, 3.5)	0.7026 (0.5018, 0.9840) 0.0400	0.0394	
PR	48	33 (68.8)	15 (31.3)	4.1 (1.4, 9.0)	21	15 (71.4)	6 (28.6)	0.3 (0.3, 2.2)	0.5353 (0.2864, 1.0005) 0.0502	0.0538	
SD	82	57 (69.5)	25 (30.5)	2.2 (0.7, 4.3)	54	35 (64.8)	19 (35.2)	0.6 (0.4, 3.3)	0.8722 (0.5704, 1.3336) 0.5279	0.5359	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Reported history of CNS metastases											0.1922
Yes	37	23 (62.2)	14 (37.8)	2.8 (0.7, NE)	13	10 (76.9)	3 (23.1)	0.4 (0.3, 1.4)	0.5257 (0.2441, 1.1322)	0.1048	
No	334	228 (68.3)	106 (31.7)	3.0 (2.2, 4.1)	159	104 (65.4)	55 (34.6)	0.7 (0.5, 1.8)	0.7473 (0.5912, 0.9447)	0.0156	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.4650
Yes	24	15 (62.5)	9 (37.5)	1.4 (0.3, NE)	7	6 (85.7)	1 (14.3)	1.0 (0.3, 3.9)	0.5768 (0.2166, 1.5365) 0.2710	0.2447	
No	347	236 (68.0)	111 (32.0)	3.0 (2.2, 4.1)	165	108 (65.5)	57 (34.5)	0.7 (0.5, 1.4)	0.7335 (0.5826, 0.9233) 0.0083	0.0093	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.4435
Normal Function	201	140 (69.7)	61 (30.3)	2.8 (1.4, 4.1)	80	48 (60.0)	32 (40.0)	0.9 (0.5, 6.9)	0.8645 (0.6211, 1.2032) 0.3879	0.4136	
Mild Impairment	123	79 (64.2)	44 (35.8)	3.4 (1.8, 4.9)	65	44 (67.7)	21 (32.3)	0.5 (0.5, 1.2)	0.6688 (0.4603, 0.9719) 0.0349	0.0385	
Moderate Impairment	41	29 (70.7)	12 (29.3)	3.5 (0.7, 6.3)	23	18 (78.3)	5 (21.7)	0.7 (0.2, 5.3)	0.5983 (0.3279, 1.0917) 0.0941	0.0943	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.3549
Normal Function	170	111 (65.3)	59 (34.7)	4.2 (2.8, 6.2)	88	59 (67.0)	29 (33.0)	0.7 (0.5, 1.8)	0.6453 (0.4682, 0.8894) 0.0075	0.0070	
Mild Impairment	194	135 (69.6)	59 (30.4)	2.7 (1.4, 3.4)	82	53 (64.6)	29 (35.4)	0.7 (0.4, 2.7)	0.8146 (0.5913, 1.1224) 0.2099	0.2333	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.3057
Yes	331	226 (68.3)	105 (31.7)	3.0 (2.2, 4.0)	146	96 (65.8)	50 (34.2)	0.7 (0.5, 1.8)	0.7516 (0.5906, 0.9566) 0.0203	0.0232	
No	40	25 (62.5)	15 (37.5)	2.2 (0.7, 19.4)	26	18 (69.2)	8 (30.8)	0.5 (0.3, 3.3)	0.5806 (0.3098, 1.0882) 0.0898	0.0750	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.6202
Positive	329	222 (67.5)	107 (32.5)	3.0 (2.1, 4.1)	152	102 (67.1)	50 (32.9)	0.5 (0.5, 1.0)	0.7139 (0.5635, 0.9046) 0.0053	0.0057	
Negative	42	29 (69.0)	13 (31.0)	2.8 (1.6, 6.2)	20	12 (60.0)	8 (40.0)	1.3 (0.5, NE)	0.7427 (0.3676, 1.5006) 0.4072	0.3973	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (derived)											0.6819
Positive	331	223 (67.4)	108 (32.6)	3.0 (2.1, 4.2)	155	102 (65.8)	53 (34.2)	0.7 (0.5, 1.8)	0.7354 (0.5804, 0.9319)	0.0116	
Negative	40	28 (70.0)	12 (30.0)	2.7 (1.6, 4.2)	17	12 (70.6)	5 (29.4)	0.9 (0.3, NE)	0.5261 (0.2561, 1.0807)	0.0763	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0975
HER2 IHC 1+	214	49 (22.9)	165 (77.1)	NE (NE, NE)	100	28 (28.0)	72 (72.0)	NE (6.9, NE)	0.6099 (0.3802, 0.9785) 0.0403	0.0386	
HER2 IHC 2+/ISH Negative	157	43 (27.4)	114 (72.6)	NE (NE, NE)	72	14 (19.4)	58 (80.6)	NE (13.6, NE)	1.0698 (0.5803, 1.9719) 0.8289	0.8307	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.8447
1	220	60 (27.3)	160 (72.7)	NE (NE, NE)	94	25 (26.6)	69 (73.4)	NE (NE, NE)	0.7978 (0.4971, 1.2806) 0.3495	0.3501	
>=2	150	32 (21.3)	118 (78.7)	NE (NE, NE)	78	17 (21.8)	61 (78.2)	NE (13.6, NE)	0.6920 (0.3800, 1.2600) 0.2286	0.2253	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.0047
Yes	233	44 (18.9)	189 (81.1)	NE (NE, NE)	112	29 (25.9)	83 (74.1)	NE (6.9, NE)	0.5127 (0.3164, 0.8307) 0.0067	0.0058	
No	98	37 (37.8)	61 (62.2)	NE (9.7, NE)	43	8 (18.6)	35 (81.4)	NE (13.6, NE)	1.7885 (0.8301, 3.8534) 0.1377	0.1324	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9992
<65	289	72 (24.9)	217 (75.1)	NE (NE, NE)	126	30 (23.8)	96 (76.2)	NE (13.6, NE)	0.7675 (0.4976, 1.1838) 0.2314	0.2277	
>=65	82	20 (24.4)	62 (75.6)	NE (14.9, NE)	46	12 (26.1)	34 (73.9)	NE (6.9, NE)	0.7469 (0.3611, 1.5445) 0.4311	0.4326	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2032
<75	357	86 (24.1)	271 (75.9)	NE (NE, NE)	163	40 (24.5)	123 (75.5)	NE (13.6, NE)	0.7303 (0.4984, 1.0701) 0.1069	0.1047	
>=75	14	6 (42.9)	8 (57.1)	8.7 (3.0, NE)	9	2 (22.2)	7 (77.8)	NE (1.0, NE)	1.9222 (0.3865, 9.5603) 0.4246	0.4165	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.4225
White	175	37 (21.1)	138 (78.9)	NE (NE, NE)	85	15 (17.6)	70 (82.4)	NE (13.6, NE)	0.8543 (0.4635, 1.5744) 0.6136	0.6113	
Non-White	196	55 (28.1)	141 (71.9)	NE (NE, NE)	86	27 (31.4)	59 (68.6)	NE (6.9, NE)	0.6823 (0.4274, 1.0893) 0.1092	0.1071	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.5934
Asia	147	48 (32.7)	99 (67.3)	NE (14.9, NE)	63	21 (33.3)	42 (66.7)	NE (4.4, NE)	0.7049 (0.4181, 1.1884) 0.1894	0.1903	
North America	58	11 (19.0)	47 (81.0)	NE (NE, NE)	28	3 (10.7)	25 (89.3)	NE (NE, NE)	1.3604 (0.3751, 4.9339) 0.6397	0.6381	
Europe + Israel	166	33 (19.9)	133 (80.1)	NE (NE, NE)	81	18 (22.2)	63 (77.8)	NE (13.6, NE)	0.6668 (0.3715, 1.1968) 0.1744	0.1707	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.2936
0	199	50 (25.1)	149 (74.9)	NE (NE, NE)	95	19 (20.0)	76 (80.0)	NE (13.6, NE)	0.9303 (0.5440, 1.5909) 0.7918	0.7867	
1	172	42 (24.4)	130 (75.6)	NE (NE, NE)	77	23 (29.9)	54 (70.1)	NE (5.5, NE)	0.6302 (0.3757, 1.0571) 0.0802	0.0785	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.2901
0	60	16 (26.7)	44 (73.3)	NE (8.6, NE)	31	5 (16.1)	26 (83.9)	NE (NE, NE)	1.1447 (0.4110, 3.1880) 0.7959	0.7961	
1	107	32 (29.9)	75 (70.1)	NE (NE, NE)	48	13 (27.1)	35 (72.9)	NE (6.9, NE)	0.9375 (0.4908, 1.7908) 0.8449	0.8382	
2	114	25 (21.9)	89 (78.1)	NE (NE, NE)	50	11 (22.0)	39 (78.0)	NE (NE, NE)	0.7705 (0.3734, 1.5901) 0.4807	0.4731	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	19 (21.1)	71 (78.9)	NE (NE, NE)	43	13 (30.2)	30 (69.8)	NE (5.5, NE)	0.4562 (0.2188, 0.9511) 0.0363	0.0323	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.6311
PD	173	37 (21.4)	136 (78.6)	NE (NE, NE)	77	17 (22.1)	60 (77.9)	NE (NE, NE)	0.7530 (0.4209, 1.3474)	0.3341	
PR	48	10 (20.8)	38 (79.2)	NE (13.2, NE)	21	6 (28.6)	15 (71.4)	NE (3.4, NE)	0.3393 (0.1186, 1.0742)	0.0564	
SD	82	23 (28.0)	59 (72.0)	NE (NE, NE)	54	14 (25.9)	40 (74.1)	NE (NE, NE)	0.3569 (0.0668, 0.8962)	0.7619	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.5359
Yes	37	8 (21.6)	29 (78.4)	NE (13.2, NE)	13	4 (30.8)	9 (69.2)	NE (2.8, NE)	0.5212 (0.1530, 1.7755)	0.2802	
No	334	84 (25.1)	250 (74.9)	NE (NE, NE)	159	38 (23.9)	121 (76.1)	NE (13.6, NE)	0.7907 (0.5358, 1.1670)	0.2368	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.6090
Yes	24	6 (25.0)	18 (75.0)	NE (13.2, NE)	7	3 (42.9)	4 (57.1)	NE (1.4, NE)	0.6124 (0.1523, 2.4621) 0.4897	0.4675	
No	347	86 (24.8)	261 (75.2)	NE (NE, NE)	165	39 (23.6)	126 (76.4)	NE (13.6, NE)	0.7769 (0.5287, 1.1415) 0.1985	0.1982	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.6041
Normal Function	201	52 (25.9)	149 (74.1)	NE (NE, NE)	80	17 (21.3)	63 (78.8)	NE (NE, NE)	0.9639 (0.5529, 1.6803) 0.8968	0.8889	
Mild Impairment	123	30 (24.4)	93 (75.6)	NE (NE, NE)	65	14 (21.5)	51 (78.5)	NE (NE, NE)	0.7763 (0.4058, 1.4852) 0.4443	0.4468	
Moderate Impairment	41	10 (24.4)	31 (75.6)	NE (11.4, NE)	23	9 (39.1)	14 (60.9)	13.6 (3.3, NE)	0.5285 (0.2141, 1.3045) 0.1665	0.1597	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.4295
Normal Function	170	40 (23.5)	130 (76.5)	NE (NE, NE)	88	18 (20.5)	70 (79.5)	NE (13.6, NE)	0.8989 (0.5105, 1.5829) 0.7121	0.7082	
Mild Impairment	194	49 (25.3)	145 (74.7)	NE (NE, NE)	82	23 (28.0)	59 (72.0)	NE (6.9, NE)	0.6297 (0.3802, 1.0431) 0.0725	0.0707	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.7724
Yes	331	80 (24.2)	251 (75.8)	NE (NE, NE)	146	36 (24.7)	110 (75.3)	NE (13.6, NE)	0.7523 (0.5048, 1.1212) 0.1621	0.1607	
No	40	12 (30.0)	28 (70.0)	NE (7.9, NE)	26	6 (23.1)	20 (76.9)	NE (3.3, NE)	0.7895 (0.2813, 2.2155) 0.6535	0.6523	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.7163
Positive	329	80 (24.3)	249 (75.7)	NE (NE, NE)	152	37 (24.3)	115 (75.7)	NE (13.6, NE)	0.7502 (0.5051, 1.1143)	0.1536	
Negative	42	12 (28.6)	30 (71.4)	NE (8.7, NE)	20	5 (25.0)	15 (75.0)	NE (3.3, NE)	0.8202 (0.2757, 2.4402)	0.7251	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.8796
Positive	331	81 (24.5)	250 (75.5)	NE (NE, NE)	155	37 (23.9)	118 (76.1)	NE (13.6, NE)	0.7723 (0.5203, 1.1464)	0.1993	
Negative	40	11 (27.5)	29 (72.5)	NE (8.7, NE)	17	5 (29.4)	12 (70.6)	NE (2.2, NE)	0.6203 (0.2044, 1.8825)	0.3978	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.2073
HER2 IHC 1+	214	53 (24.8)	161 (75.2)	NE (NE, NE)	100	35 (35.0)	65 (65.0)	NE (NE, NE)	0.4859 (0.3153, 0.7487) 0.0011	0.0009	
HER2 IHC 2+/ISH Negative	157	28 (17.8)	129 (82.2)	24.8 (24.8, NE)	72	27 (37.5)	45 (62.5)	NE (3.5, NE)	0.3150 (0.1832, 0.5414) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.4543
1	220	48 (21.8)	172 (78.2)	NE (NE, NE)	94	31 (33.0)	63 (67.0)	NE (6.9, NE)	0.4533 (0.2870, 0.7160) 0.0007	0.0005	
>=2	150	33 (22.0)	117 (78.0)	24.8 (24.8, NE)	78	31 (39.7)	47 (60.3)	NE (2.4, NE)	0.3739 (0.2266, 0.6168) 0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.7798
Yes	233	40 (17.2)	193 (82.8)	NE (NE, NE)	112	35 (31.3)	77 (68.8)	NE (NE, NE)	0.4080 (0.2581, 0.6449) 0.0001	<0.0001	
No	98	35 (35.7)	63 (64.3)	24.8 (10.6, 24.8)	43	23 (53.5)	20 (46.5)	3.5 (0.5, NE)	0.4055 (0.2382, 0.6904) 0.0009	0.0007	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6467
<65	289	67 (23.2)	222 (76.8)	24.8 (24.8, NE)	126	45 (35.7)	81 (64.3)	NE (NE, NE)	0.4189 (0.2851, 0.6154) <0.0001	<0.0001	
>=65	82	14 (17.1)	68 (82.9)	NE (NE, NE)	46	17 (37.0)	29 (63.0)	NE (3.0, NE)	0.3539 (0.1733, 0.7227) 0.0043	0.0030	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8769
<75	357	79 (22.1)	278 (77.9)	24.8 (24.8, NE)	163	59 (36.2)	104 (63.8)	NE (6.9, NE)	0.4087 (0.2900, 0.5760) <0.0001	<0.0001	
>=75	14	2 (14.3)	12 (85.7)	NE (6.9, NE)	9	3 (33.3)	6 (66.7)	NE (0.2, NE)	0.3500 (0.0581, 2.1099) 0.2521	0.2311	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.7786
White	175	15 (8.6)	160 (91.4)	NE (NE, NE)	85	14 (16.5)	71 (83.5)	NE (NE, NE)	0.4059 (0.1942, 0.8485) 0.0165	0.0138	
Non-White	196	66 (33.7)	130 (66.3)	24.8 (11.8, NE)	86	48 (55.8)	38 (44.2)	1.0 (0.5, NE)	0.3447 (0.2361, 0.5033) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.0499
Asia	147	59 (40.1)	88 (59.9)	24.8 (9.7, NE)	63	45 (71.4)	18 (28.6)	0.5 (0.3, 0.5)	0.2554 (0.1714, 0.3805) <0.0001	<0.0001	
North America	58	10 (17.2)	48 (82.8)	NE (NE, NE)	28	12 (42.9)	16 (57.1)	NE (0.5, NE)	0.2396 (0.0998, 0.5752) 0.0014	0.0006	
Europe + Israel	166	12 (7.2)	154 (92.8)	NE (NE, NE)	81	5 (6.2)	76 (93.8)	NE (NE, NE)	0.9641 (0.3356, 2.7696) 0.9459	0.9453	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											
0	199	52 (26.1)	147 (73.9)	NE (NE, NE)	95	31 (32.6)	64 (67.4)	NE (NE, NE)	0.5311 (0.3388, 0.8324) 0.0058	0.0056	0.0748
1	172	29 (16.9)	143 (83.1)	24.8 (NE, NE)	77	31 (40.3)	46 (59.7)	6.9 (2.4, NE)	0.2967 (0.1767, 0.4982) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.7740
0	60	11 (18.3)	49 (81.7)	NE (NE, NE)	31	11 (35.5)	20 (64.5)	6.9 (2.4, NE)	0.3143 (0.1325, 0.7458) 0.0087	0.0058	
1	107	26 (24.3)	81 (75.7)	NE (NE, NE)	48	17 (35.4)	31 (64.6)	NE (3.5, NE)	0.5289 (0.2865, 0.9763) 0.0417	0.0388	
2	114	21 (18.4)	93 (81.6)	NE (NE, NE)	50	15 (30.0)	35 (70.0)	NE (NE, NE)	0.4260 (0.2166, 0.8379) 0.0134	0.0121	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	23 (25.6)	67 (74.4)	24.8 (24.8, NE)	43	19 (44.2)	24 (55.8)	NE (0.5, NE)	0.3440 (0.1841, 0.6427) 0.0008	0.0006	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.4229
PD	173	33 (19.1)	140 (80.9)	NE (NE, NE)	77	24 (31.2)	53 (68.8)	NE (6.9, NE)	0.4386 (0.2577, 0.7464)	0.0019	
PR	48	11 (22.9)	37 (77.1)	24.8 (NE, NE)	21	10 (47.6)	11 (52.4)	NE (0.3, NE)	0.2214 (0.0889, 0.5514)	0.0005	
SD	82	20 (24.4)	62 (75.6)	NE (NE, NE)	54	22 (40.7)	32 (59.3)	NE (1.4, NE)	0.4704 (0.2561, 0.8641)	0.0137	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Reported history of CNS metastases											0.8307
Yes	37	10 (27.0)	27 (73.0)	NE (NE, NE)	13	5 (38.5)	8 (61.5)	NE (0.3, NE)	0.4704 (0.1586, 1.3957)	0.1757	
No	334	71 (21.3)	263 (78.7)	24.8 (24.8, NE)	159	57 (35.8)	102 (64.2)	NE (6.9, NE)	0.3999 (0.2805, 0.5700)	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.1509
Yes	24	9 (37.5)	15 (62.5)	NE (4.2, NE)	7	2 (28.6)	5 (71.4)	NE (0.3, NE)	1.1276 (0.2421, 5.2510) 0.8784	0.8765	
No	347	72 (20.7)	275 (79.3)	24.8 (24.8, NE)	165	60 (36.4)	105 (63.6)	NE (6.9, NE)	0.3817 (0.2694, 0.5409) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Renal function at baseline											0.1044
Normal Function	201	48 (23.9)	153 (76.1)	NE (NE, NE)	80	27 (33.8)	53 (66.3)	NE (6.9, NE)	0.4478 (0.2765, 0.7252) 0.0011	0.0009	
Mild Impairment	123	28 (22.8)	95 (77.2)	24.8 (24.8, NE)	65	22 (33.8)	43 (66.2)	NE (NE, NE)	0.4748 (0.2690, 0.8378) 0.0102	0.0100	
Moderate Impairment	41	3 (7.3)	38 (92.7)	NE (NE, NE)	23	10 (43.5)	13 (56.5)	NE (0.9, NE)	0.1246 (0.0341, 0.4550) 0.0016	0.0002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.0597
Normal Function	170	36 (21.2)	134 (78.8)	NE (24.8, NE)	88	38 (43.2)	50 (56.8)	NE (2.4, NE)	0.3101 (0.1945, 0.4944) <0.0001	<0.0001	
Mild Impairment	194	43 (22.2)	151 (77.8)	NE (NE, NE)	82	22 (26.8)	60 (73.2)	NE (NE, NE)	0.5958 (0.3543, 1.0019) 0.0508	0.0538	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.2888
Yes	331	72 (21.8)	259 (78.2)	24.8 (NE, NE)	146	50 (34.2)	96 (65.8)	NE (NE, NE)	0.4398 (0.3051, 0.6340) <0.0001	<0.0001	
No	40	9 (22.5)	31 (77.5)	NE (NE, NE)	26	12 (46.2)	14 (53.8)	3.3 (0.5, NE)	0.2688 (0.1091, 0.6621) 0.0043	0.0024	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.8466
Positive	329	75 (22.8)	254 (77.2)	24.8 (24.8, NE)	152	57 (37.5)	95 (62.5)	NE (6.9, NE)	0.4048 (0.2854, 0.5742) <0.0001	<0.0001	
Negative	42	6 (14.3)	36 (85.7)	NE (NE, NE)	20	5 (25.0)	15 (75.0)	NE (2.4, NE)	0.3692 (0.1081, 1.2611) 0.1119	0.0991	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.5597
Positive	331	74 (22.4)	257 (77.6)	24.8 (24.8, NE)	155	58 (37.4)	97 (62.6)	NE (6.9, NE)	0.3996 (0.2819, 0.5664)	<0.0001	
Negative	40	7 (17.5)	33 (82.5)	NE (NE, NE)	17	4 (23.5)	13 (76.5)	NE (2.4, NE)	0.4827 (0.1363, 1.7095)	0.2494	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.3924
HER2 IHC 1+	214	51 (23.8)	163 (76.2)	NE (NE, NE)	100	29 (29.0)	71 (71.0)	NE (NE, NE)	0.5948 (0.3745, 0.9448) 0.0278	0.0284	
HER2 IHC 2+/ISH Negative	157	27 (17.2)	130 (82.8)	24.8 (24.8, NE)	72	20 (27.8)	52 (72.2)	NE (NE, NE)	0.4527 (0.2513, 0.8156) 0.0083	0.0072	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.4931
1	220	42 (19.1)	178 (80.9)	NE (NE, NE)	94	22 (23.4)	72 (76.6)	NE (NE, NE)	0.6115 (0.3631, 1.0298) 0.0644	0.0632	
>=2	150	36 (24.0)	114 (76.0)	24.8 (19.4, NE)	78	27 (34.6)	51 (65.4)	NE (NE, NE)	0.4814 (0.2889, 0.8021) 0.0050	0.0048	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											
Yes	233	34 (14.6)	199 (85.4)	NE (NE, NE)	112	25 (22.3)	87 (77.7)	NE (NE, NE)	0.5239 (0.3111, 0.8823) 0.0151	0.0140	0.4530
No	98	35 (35.7)	63 (64.3)	24.8 (9.2, 24.8)	43	17 (39.5)	26 (60.5)	NE (0.5, NE)	0.6416 (0.3578, 1.1507) 0.1365	0.1400	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8758
<65	289	63 (21.8)	226 (78.2)	24.8 (24.8, NE)	126	36 (28.6)	90 (71.4)	NE (NE, NE)	0.5329 (0.3512, 0.8086) 0.0031	0.0030	
>=65	82	15 (18.3)	67 (81.7)	NE (NE, NE)	46	13 (28.3)	33 (71.7)	NE (NE, NE)	0.5251 (0.2487, 1.1088) 0.0912	0.0858	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4832
<75	357	76 (21.3)	281 (78.7)	24.8 (24.8, NE)	163	48 (29.4)	115 (70.6)	NE (NE, NE)	0.5148 (0.3564, 0.7435) 0.0004	0.0004	
>=75	14	2 (14.3)	12 (85.7)	NE (4.2, NE)	9	1 (11.1)	8 (88.9)	NE (0.2, NE)	1.0628 (0.0954, 11.8437) 0.9605	0.9605	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.4607
White	175	14 (8.0)	161 (92.0)	NE (NE, NE)	85	13 (15.3)	72 (84.7)	NE (NE, NE)	0.4032 (0.1868, 0.8704) 0.0207	0.0173	
Non-White	196	64 (32.7)	132 (67.3)	24.8 (19.4, NE)	86	36 (41.9)	50 (58.1)	NE (1.2, NE)	0.5333 (0.3525, 0.8067) 0.0029	0.0027	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.7224
Asia	147	58 (39.5)	89 (60.5)	19.4 (8.3, NE)	63	33 (52.4)	30 (47.6)	3.2 (0.5, NE)	0.4524 (0.2929, 0.6990) 0.0004	0.0003	
North America	58	8 (13.8)	50 (86.2)	NE (NE, NE)	28	8 (28.6)	20 (71.4)	NE (NE, NE)	0.3628 (0.1342, 0.9809) 0.0457	0.0397	
Europe + Israel	166	12 (7.2)	154 (92.8)	NE (NE, NE)	81	8 (9.9)	73 (90.1)	NE (NE, NE)	0.6125 (0.2476, 1.5150) 0.2888	0.2837	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.2574
0	199	51 (25.6)	148 (74.4)	NE (NE, NE)	95	27 (28.4)	68 (71.6)	NE (NE, NE)	0.6159 (0.3842, 0.9873) 0.0441	0.0465	
1	172	27 (15.7)	145 (84.3)	24.8 (19.4, 24.8)	77	22 (28.6)	55 (71.4)	NE (NE, NE)	0.4424 (0.2494, 0.7850) 0.0053	0.0042	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.0540
0	60	13 (21.7)	47 (78.3)	NE (NE, NE)	31	11 (35.5)	20 (64.5)	NE (0.9, NE)	0.4244 (0.1878, 0.9591) 0.0394	0.0350	
1	107	24 (22.4)	83 (77.6)	NE (NE, NE)	48	13 (27.1)	35 (72.9)	NE (NE, NE)	0.6602 (0.3352, 1.3003) 0.2299	0.2265	
2	114	23 (20.2)	91 (79.8)	NE (19.4, NE)	50	7 (14.0)	43 (86.0)	NE (NE, NE)	1.1686 (0.4962, 2.7523) 0.7215	0.7206	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	18 (20.0)	72 (80.0)	NE (24.8, NE)	43	18 (41.9)	25 (58.1)	NE (0.5, NE)	0.2755 (0.1394, 0.5446) 0.0002	0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.7804
PD	173	37 (21.4)	136 (78.6)	NE (NE, NE)	77	22 (28.6)	55 (71.4)	NE (NE, NE)	0.5547 (0.3255, 0.9453)	0.0290	
PR	48	10 (20.8)	38 (79.2)	24.8 (19.4, 24.8)	21	7 (33.3)	14 (66.7)	NE (0.3, NE)	0.3448 (0.1236, 0.9618)	0.0357	
SD	82	18 (22.0)	64 (78.0)	NE (NE, NE)	54	16 (29.6)	38 (70.4)	NE (NE, NE)	0.5975 (0.3025, 1.1800)	0.1376	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.4618
Yes	37	12 (32.4)	25 (67.6)	NE (4.2, NE)	13	4 (30.8)	9 (69.2)	NE (0.4, NE)	0.8824 (0.2837, 2.7449)	0.8449	
No	334	66 (19.8)	268 (80.2)	24.8 (24.8, NE)	159	45 (28.3)	114 (71.7)	NE (NE, NE)	0.8290 (0.3372, 0.7297)	0.0003	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0619
Yes	24	9 (37.5)	15 (62.5)	NE (0.7, NE)	7	1 (14.3)	6 (85.7)	NE (0.4, NE)	2.7139 (0.3437, 21.4299) 0.3437	0.3280	
No	347	69 (19.9)	278 (80.1)	24.8 (24.8, NE)	165	48 (29.1)	117 (70.9)	NE (NE, NE)	0.4827 (0.3317, 0.7025) 0.0001	0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.2569
Normal Function	201	39 (19.4)	162 (80.6)	NE (NE, NE)	80	19 (23.8)	61 (76.3)	NE (NE, NE)	0.6095 (0.3497, 1.0625) 0.0808	0.0793	
Mild Impairment	123	31 (25.2)	92 (74.8)	24.8 (24.8, NE)	65	18 (27.7)	47 (72.3)	NE (NE, NE)	0.6839 (0.3793, 1.2331) 0.2065	0.2213	
Moderate Impairment	41	6 (14.6)	35 (85.4)	19.4 (19.4, NE)	23	9 (39.1)	14 (60.9)	NE (0.4, NE)	0.2362 (0.0788, 0.7075) 0.0099	0.0055	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.2314
Normal Function	170	40 (23.5)	130 (76.5)	24.8 (24.8, NE)	88	31 (35.2)	57 (64.8)	NE (NE, NE)	0.4629 (0.2866, 0.7478) 0.0016	0.0013	
Mild Impairment	194	36 (18.6)	158 (81.4)	NE (NE, NE)	82	16 (19.5)	66 (80.5)	NE (NE, NE)	0.7332 (0.4045, 1.3292) 0.3066	0.3160	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1112
Yes	331	68 (20.5)	263 (79.5)	24.8 (NE, NE)	146	37 (25.3)	109 (74.7)	NE (NE, NE)	0.6192 (0.4132, 0.9279) 0.0202	0.0206	
No	40	10 (25.0)	30 (75.0)	NE (19.4, NE)	26	12 (46.2)	14 (53.8)	NE (0.4, NE)	0.2716 (0.1096, 0.6734) 0.0049	0.0030	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.7942
Positive	329	68 (20.7)	261 (79.3)	24.8 (24.8, NE)	152	43 (28.3)	109 (71.7)	NE (NE, NE)	0.5332 (0.3621, 0.7850)	0.0013	
Negative	42	10 (23.8)	32 (76.2)	19.4 (8.5, NE)	20	6 (30.0)	14 (70.0)	NE (0.9, NE)	0.4982 (0.1705, 1.4555)	0.1952	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.4800
Positive	331	69 (20.8)	262 (79.2)	24.8 (24.8, NE)	155	42 (27.1)	113 (72.9)	NE (NE, NE)	0.5594 (0.3788, 0.8261)	0.0035	0.0033
Negative	40	9 (22.5)	31 (77.5)	NE (8.5, NE)	17	7 (41.2)	10 (58.8)	NE (0.5, NE)	0.3198 (0.1132, 0.9033)	0.0314	0.0249

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0481
HER2 IHC 1+	214	42 (19.6)	172 (80.4)	NE (NE, NE)	100	31 (31.0)	69 (69.0)	NE (NE, NE)	0.4810 (0.2997, 0.7720) 0.0024	0.0020	
HER2 IHC 2+/ISH Negative	157	33 (21.0)	124 (79.0)	NE (NE, NE)	72	12 (16.7)	60 (83.3)	NE (13.6, NE)	1.0523 (0.5400, 2.0506) 0.8809	0.8872	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.9338
1	220	50 (22.7)	170 (77.3)	NE (NE, NE)	94	27 (28.7)	67 (71.3)	NE (NE, NE)	0.6355 (0.3952, 1.0218) 0.0614	0.0609	
>=2	150	25 (16.7)	125 (83.3)	NE (NE, NE)	78	16 (20.5)	62 (79.5)	NE (13.6, NE)	0.6237 (0.3298, 1.1797) 0.1466	0.1427	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.0678
Yes	233	39 (16.7)	194 (83.3)	NE (NE, NE)	112	29 (25.9)	83 (74.1)	NE (NE, NE)	0.5116 (0.3141, 0.8333) 0.0071	0.0062	
No	98	29 (29.6)	69 (70.4)	NE (NE, NE)	43	10 (23.3)	33 (76.7)	NE (13.6, NE)	1.0827 (0.5249, 2.2334) 0.8297	0.8319	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3179
<65	289	60 (20.8)	229 (79.2)	NE (NE, NE)	126	35 (27.8)	91 (72.2)	NE (13.6, NE)	0.5609 (0.3668, 0.8576) 0.0076	0.0068	
>=65	82	15 (18.3)	67 (81.7)	NE (NE, NE)	46	8 (17.4)	38 (82.6)	NE (NE, NE)	0.9727 (0.4103, 2.3060) 0.9499	0.9550	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6978
<75	357	72 (20.2)	285 (79.8)	NE (NE, NE)	163	41 (25.2)	122 (74.8)	NE (13.6, NE)	0.6295 (0.4263, 0.9297) 0.0200	0.0189	
>=75	14	3 (21.4)	11 (78.6)	NE (3.0, NE)	9	2 (22.2)	7 (77.8)	NE (0.5, NE)	0.9007 (0.1500, 5.4074) 0.9089	0.9089	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.7733
White	175	29 (16.6)	146 (83.4)	NE (NE, NE)	85	17 (20.0)	68 (80.0)	NE (13.6, NE)	0.6765 (0.3687, 1.2412) 0.2069	0.2057	
Non-White	196	46 (23.5)	150 (76.5)	NE (NE, NE)	86	26 (30.2)	60 (69.8)	NE (5.6, NE)	0.6016 (0.3692, 0.9803) 0.0414	0.0390	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.5709
Asia	147	39 (26.5)	108 (73.5)	NE (NE, NE)	63	23 (36.5)	40 (63.5)	NE (4.0, NE)	0.5203 (0.3076, 0.8801) 0.0148	0.0131	
North America	58	6 (10.3)	52 (89.7)	NE (NE, NE)	28	2 (7.1)	26 (92.9)	NE (NE, NE)	1.0406 (0.2042, 5.3018) 0.9618	0.9582	
Europe + Israel	166	30 (18.1)	136 (81.9)	NE (NE, NE)	81	18 (22.2)	63 (77.8)	NE (13.6, NE)	0.7071 (0.3919, 1.2759) 0.2497	0.2461	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.5984
0	199	42 (21.1)	157 (78.9)	NE (NE, NE)	95	22 (23.2)	73 (76.8)	NE (13.6, NE)	0.7036 (0.4171, 1.1869) 0.1876	0.1886	
1	172	33 (19.2)	139 (80.8)	NE (NE, NE)	77	21 (27.3)	56 (72.7)	NE (5.5, NE)	0.5851 (0.3359, 1.0192) 0.0584	0.0546	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.9258
0	60	11 (18.3)	49 (81.7)	NE (NE, NE)	31	7 (22.6)	24 (77.4)	NE (4.0, NE)	0.6383 (0.2427, 1.6788)	0.3609	
1	107	27 (25.2)	80 (74.8)	NE (NE, NE)	48	15 (31.3)	33 (68.8)	NE (13.6, NE)	0.6843 (0.3633, 1.2889)	0.2352	
2	114	22 (19.3)	92 (80.7)	NE (NE, NE)	50	11 (22.0)	39 (78.0)	NE (5.6, NE)	0.7381 (0.3540, 1.5388)	0.4139	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	15 (16.7)	75 (83.3)	NE (NE, NE)	43	10 (23.3)	33 (76.7)	NE (5.5, NE)	0.4910 (0.2146, 1.1237) 0.0922	0.0869	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.6316
PD	173	34 (19.7)	139 (80.3)	NE (NE, NE)	77	18 (23.4)	59 (76.6)	NE (NE, NE)	0.6574 (0.3682, 1.1737)	0.1534	
PR	48	9 (18.8)	39 (81.3)	NE (NE, NE)	21	7 (33.3)	14 (66.7)	NE (3.4, NE)	0.3753 (0.1327, 1.0614)	0.0546	
SD	82	16 (19.5)	66 (80.5)	NE (NE, NE)	54	12 (22.2)	42 (77.8)	NE (NE, NE)	0.7751 (0.3647, 1.6474)	0.5028	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.6286
Yes	37	6 (16.2)	31 (83.8)	NE (NE, NE)	13	2 (15.4)	11 (84.6)	NE (2.8, NE)	0.9563 (0.1914, 4.7777)	0.9325	
No	334	69 (20.7)	265 (79.3)	NE (NE, NE)	159	41 (25.8)	118 (74.2)	NE (13.6, NE)	0.9566 (0.4235, 0.9282)	0.6270 (0.0197)	0.0191

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.6411
Yes	24	6 (25.0)	18 (75.0)	NE (NE, NE)	7	2 (28.6)	5 (71.4)	NE (2.8, NE)	0.9634 (0.1943, 4.7767) 0.9636	0.9282	
No	347	69 (19.9)	278 (80.1)	NE (NE, NE)	165	41 (24.8)	124 (75.2)	NE (13.6, NE)	0.6223 (0.4203, 0.9216) 0.0179	0.0173	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.8540
Normal Function	201	48 (23.9)	153 (76.1)	NE (NE, NE)	80	23 (28.8)	57 (71.3)	NE (5.6, NE)	0.6643 (0.4010, 1.1005) 0.1123	0.1081	
Mild Impairment	123	21 (17.1)	102 (82.9)	NE (NE, NE)	65	12 (18.5)	53 (81.5)	NE (NE, NE)	0.7333 (0.3573, 1.5049) 0.3977	0.3982	
Moderate Impairment	41	6 (14.6)	35 (85.4)	NE (NE, NE)	23	6 (26.1)	17 (73.9)	NE (13.6, NE)	0.4721 (0.1511, 1.4747) 0.1965	0.1843	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.9503
Normal Function	170	28 (16.5)	142 (83.5)	NE (NE, NE)	88	18 (20.5)	70 (79.5)	NE (13.6, NE)	0.6359 (0.3478, 1.1626) 0.1414	0.1372	
Mild Impairment	194	46 (23.7)	148 (76.3)	NE (NE, NE)	82	24 (29.3)	58 (70.7)	NE (5.6, NE)	0.6322 (0.3834, 1.0425) 0.0723	0.0706	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.6763
Yes	331	65 (19.6)	266 (80.4)	NE (NE, NE)	146	37 (25.3)	109 (74.7)	NE (13.6, NE)	0.6283 (0.4176, 0.9452) 0.0257	0.0247	
No	40	10 (25.0)	30 (75.0)	NE (10.4, NE)	26	6 (23.1)	20 (76.9)	NE (4.0, NE)	0.7640 (0.2685, 2.1734) 0.6138	0.6098	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.8554
Positive	329	68 (20.7)	261 (79.3)	NE (NE, NE)	152	39 (25.7)	113 (74.3)	NE (13.6, NE)	0.6360 (0.4267, 0.9479)	0.0254	
Negative	42	7 (16.7)	35 (83.3)	NE (NE, NE)	20	4 (20.0)	16 (80.0)	NE (4.0, NE)	0.7215 (0.2069, 2.5158)	0.6103	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.9384
Positive	331	68 (20.5)	263 (79.5)	NE (NE, NE)	155	39 (25.2)	116 (74.8)	NE (13.6, NE)	0.6474 (0.4343, 0.9650)	0.0318	
Negative	40	7 (17.5)	33 (82.5)	NE (NE, NE)	17	4 (23.5)	13 (76.5)	NE (4.0, NE)	0.6219 (0.1777, 2.1768)	0.4569	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.1996
HER2 IHC 1+	214	44 (20.6)	170 (79.4)	NE (NE, NE)	100	5 (5.0)	95 (95.0)	NE (NE, NE)	3.4592 (1.3648, 8.7678) 0.0089	0.0056	
HER2 IHC 2+/ISH Negative	157	29 (18.5)	128 (81.5)	NE (NE, NE)	72	7 (9.7)	65 (90.3)	NE (NE, NE)	1.5055 (0.6531, 3.4707) 0.3370	0.3340	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting									0.4946
1	220	35 (15.9)	185 (84.1)	94	4 (4.3)	90 (95.7)	NE (NE, NE)	2.9940 (1.0579, 8.4730) 0.0388	0.0308
>=2	150	38 (25.3)	112 (74.7)	78	8 (10.3)	70 (89.7)	NE (NE, NE)	2.0828 (0.9636, 4.5020) 0.0621	0.0577

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.8594
Yes	233	39 (16.7)	194 (83.3)	NE (NE, NE)	112	5 (4.5)	107 (95.5)	NE (NE, NE)	2.9864 (1.1679, 7.6364) 0.0224	0.0168	
No	98	28 (28.6)	70 (71.4)	NE (NE, NE)	43	4 (9.3)	39 (90.7)	NE (NE, NE)	2.7272 (0.9522, 7.8105) 0.0617	0.0527	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0564
<65	289	60 (20.8)	229 (79.2)	NE (NE, NE)	126	6 (4.8)	120 (95.2)	NE (NE, NE)	3.4583 (1.4861, 8.0477) 0.0040	0.0022	
>=65	82	13 (15.9)	69 (84.1)	NE (NE, NE)	46	6 (13.0)	40 (87.0)	NE (NE, NE)	1.0966 (0.4126, 2.9149) 0.8533	0.8565	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0038
<75	357	71 (19.9)	286 (80.1)	NE (NE, NE)	163	8 (4.9)	155 (95.1)	NE (NE, NE)	3.3409 (1.6015, 6.9695) 0.0013	0.0006	
>=75	14	2 (14.3)	12 (85.7)	NE (4.0, NE)	9	4 (44.4)	5 (55.6)	NE (0.5, NE)	0.2168 (0.0384, 1.2246) 0.0835	0.0593	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.0780
White	175	18 (10.3)	157 (89.7)	NE (NE, NE)	85	6 (7.1)	79 (92.9)	NE (NE, NE)	1.0917 (0.4266, 2.7938) 0.8548	0.8558	
Non-White	196	55 (28.1)	141 (71.9)	NE (NE, NE)	86	6 (7.0)	80 (93.0)	NE (NE, NE)	3.4549 (1.4816, 8.0560) 0.0041	0.0023	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.3024
Asia	147	51 (34.7)	96 (65.3)	NE (12.8, NE)	63	6 (9.5)	57 (90.5)	NE (NE, NE)	3.2337 (1.3820, 7.5666) 0.0068	0.0044	
North America	58	7 (12.1)	51 (87.9)	NE (NE, NE)	28	3 (10.7)	25 (89.3)	NE (NE, NE)	0.9457 (0.2433, 3.6756) 0.9358	0.9354	
Europe + Israel	166	15 (9.0)	151 (91.0)	NE (NE, NE)	81	3 (3.7)	78 (96.3)	NE (NE, NE)	1.6409 (0.4644, 5.7972) 0.4419	0.4369	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											
0	199	46 (23.1)	153 (76.9)	NE (NE, NE)	95	7 (7.4)	88 (92.6)	NE (NE, NE)	2.6572 (1.1929, 5.9186) 0.0168	0.0134	0.6915
1	172	27 (15.7)	145 (84.3)	NE (NE, NE)	77	5 (6.5)	72 (93.5)	NE (NE, NE)	1.8742 (0.7133, 4.9243) 0.2025	0.1972	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.4490
0	60	7 (11.7)	53 (88.3)	NE (NE, NE)	31	3 (9.7)	28 (90.3)	NE (NE, NE)	1.1499 (0.2966, 4.4576) 0.8399	0.8528	
1	107	25 (23.4)	82 (76.6)	NE (NE, NE)	48	3 (6.3)	45 (93.8)	NE (NE, NE)	3.3244 (1.0021, 11.0280) 0.0496	0.0375	
2	114	22 (19.3)	92 (80.7)	NE (NE, NE)	50	2 (4.0)	48 (96.0)	NE (NE, NE)	3.5989 (0.8323, 15.5613) 0.0865	0.0684	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	19 (21.1)	71 (78.9) (NE, NE)	43	4 (9.3)	39 (90.7) (NE, NE)	1.9330 (0.6491, 5.7564) 0.2365	0.2311	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.6353
PD	173	29 (16.8)	144 (83.2)	NE (NE, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	3.5413 (1.0728, 11.6901) 0.0380	0.0269	
PR	48	9 (18.8)	39 (81.3)	NE (NE, NE)	21	1 (4.8)	20 (95.2)	NE (NE, NE)	3.8182 (0.4826, 30.2103) 0.2043	0.1725	
SD	82	16 (19.5)	66 (80.5)	NE (NE, NE)	54	5 (9.3)	49 (90.7)	NE (NE, NE)	1.8407 (0.6661, 5.0860) 0.2394	0.2369	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Reported history of CNS metastases											0.4671
Yes	37	9 (24.3)	28 (75.7)	NE (NE, NE)	13	2 (15.4)	11 (84.6)	NE (NE, NE)	1.4904 (0.3206, 6.9289) 0.6107	0.6084	
No	334	64 (19.2)	270 (80.8)	NE (NE, NE)	159	10 (6.3)	149 (93.7)	NE (NE, NE)	2.4324 (1.2414, 4.7659) 0.0096	0.0078	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.2844
Yes	24	5 (20.8)	19 (79.2)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9956	0.2096	
No	347	68 (19.6)	279 (80.4)	NE (NE, NE)	165	12 (7.3)	153 (92.7)	NE (NE, NE)	2.1685 (1.1668, 4.0301) 0.0144	0.0127	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0012
Normal Function	201	39 (19.4)	162 (80.6)	NE (NE, NE)	80	2 (2.5)	78 (97.5)	NE (NE, NE)	5.7264 (1.3732, 23.8804) 0.0166	0.0067	
Mild Impairment	123	27 (22.0)	96 (78.0)	NE (NE, NE)	65	3 (4.6)	62 (95.4)	NE (NE, NE)	4.4651 (1.3489, 14.7801) 0.0143	0.0071	
Moderate Impairment	41	6 (14.6)	35 (85.4)	NE (NE, NE)	23	7 (30.4)	16 (69.6)	NE (3.7, NE)	0.3848 (0.1289, 1.1488) 0.0870	0.0765	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.9519
Normal Function	170	28 (16.5)	142 (83.5)	NE (NE, NE)	88	5 (5.7)	83 (94.3)	NE (NE, NE)	2.2869 (0.8743, 5.9823) 0.0918	0.0842	
Mild Impairment	194	44 (22.7)	150 (77.3)	NE (NE, NE)	82	7 (8.5)	75 (91.5)	NE (NE, NE)	2.1864 (0.9781, 4.8874) 0.0566	0.0529	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.9475
Yes	331	63 (19.0)	268 (81.0)	NE (NE, NE)	146	10 (6.8)	136 (93.2)	NE (NE, NE)	2.2346 (1.1403, 4.3790) 0.0192	0.0168	
No	40	10 (25.0)	30 (75.0)	NE (NE, NE)	26	2 (7.7)	24 (92.3)	NE (NE, NE)	3.1199 (0.6817, 14.2792) 0.1426	0.1227	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.0976
Positive	329	67 (20.4)	262 (79.6)	NE (NE, NE)	152	9 (5.9)	143 (94.1)	NE (NE, NE)	2.8312 (1.4052, 5.7045) 0.0036	0.0024	
Negative	42	6 (14.3)	36 (85.7)	NE (NE, NE)	20	3 (15.0)	17 (85.0)	NE (NE, NE)	0.7598 (0.1813, 3.1838) 0.7071	0.6985	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.0952
Positive	331	66 (19.9)	265 (80.1)	NE (NE, NE)	155	9 (5.8)	146 (94.2)	NE (NE, NE)	2.8325 (1.4047, 5.7116)	0.0025	
Negative	40	7 (17.5)	33 (82.5)	NE (NE, NE)	17	3 (17.6)	14 (82.4)	NE (NE, NE)	0.7344 (0.1819, 2.9646)	0.6565	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Weight decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.5460
HER2 IHC 1+	214	35 (16.4)	179 (83.6)	NE (NE, NE)	100	7 (7.0)	93 (93.0)	NE (NE, NE)	1.6029 (0.7063, 3.6377) 0.2592	0.2553	
HER2 IHC 2+/ISH Negative	157	25 (15.9)	132 (84.1)	NE (NE, NE)	72	7 (9.7)	65 (90.3)	NE (7.9, NE)	0.9838 (0.4186, 2.3122) 0.9701	0.9685	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Weight decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.5447
1	220	33 (15.0)	187 (85.0)	NE (NE, NE)	94	6 (6.4)	88 (93.6)	NE (NE, NE)	1.5203 (0.6300, 3.6686) 0.3513	0.3480	
>=2	150	27 (18.0)	123 (82.0)	NE (NE, NE)	78	8 (10.3)	70 (89.7)	NE (NE, NE)	1.1345 (0.5088, 2.5297) 0.7578	0.7588	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Weight decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											
Yes	233	33 (14.2)	200 (85.8)	NE (NE, NE)	112	7 (6.3)	105 (93.8)	NE (NE, NE)	1.4532 (0.6361, 3.3200) 0.3752	0.3734	0.9466
No	98	22 (22.4)	76 (77.6)	NE (NE, NE)	43	5 (11.6)	38 (88.4)	NE (NE, NE)	1.2729 (0.4780, 3.3897) 0.6292	0.6283	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Weight decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0431
<65	289	42 (14.5)	247 (85.5)	NE (NE, NE)	126	12 (9.5)	114 (90.5)	NE (NE, NE)	0.9565 (0.4977, 1.8383) 0.8939	0.8940	
>=65	82	18 (22.0)	64 (78.0)	NE (15.5, NE)	46	2 (4.3)	44 (95.7)	NE (NE, NE)	3.7198 (0.8572, 16.1420) 0.0794	0.0601	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Weight decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9533
<75	357	58 (16.2)	299 (83.8)	NE (NE, NE)	163	13 (8.0)	150 (92.0)	NE (NE, NE)	1.2836 (0.6972, 2.3632) 0.4226	0.4222	
>=75	14	2 (14.3)	12 (85.7)	NE (2.8, NE)	9	1 (11.1)	8 (88.9)	NE (4.6, NE)	1.3612 (0.1233, 15.0278) 0.8013	0.8005	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Weight decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.0584
White	175	28 (16.0)	147 (84.0)	NE (NE, NE)	85	3 (3.5)	82 (96.5)	NE (NE, NE)	2.9564 (0.8923, 9.7951) 0.0761	0.0630	
Non-White	196	32 (16.3)	164 (83.7)	NE (NE, NE)	86	11 (12.8)	75 (87.2)	NE (NE, NE)	0.8209 (0.4077, 1.6532) 0.5806	0.5797	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Weight decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.2344
Asia	147	27 (18.4)	120 (81.6)	NE (NE, NE)	63	9 (14.3)	54 (85.7)	NE (NE, NE)	0.7309 (0.3368, 1.5862) 0.4278	0.4255	
North America	58	10 (17.2)	48 (82.8)	NE (NE, NE)	28	2 (7.1)	26 (92.9)	NE (7.9, NE)	1.4249 (0.3051, 6.6547) 0.6525	0.6506	
Europe + Israel	166	23 (13.9)	143 (86.1)	NE (NE, NE)	81	3 (3.7)	78 (96.3)	NE (NE, NE)	2.7890 (0.8315, 9.3549) 0.0967	0.0829	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Weight decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.5247
0	199	26 (13.1)	173 (86.9)	NE (NE, NE)	95	7 (7.4)	88 (92.6)	NE (NE, NE)	1.0039 (0.4283, 2.3535) 0.9928	0.9947	
1	172	34 (19.8)	138 (80.2)	NE (NE, NE)	77	7 (9.1)	70 (90.9)	NE (7.9, NE)	1.6408 (0.7225, 3.7263) 0.2367	0.2327	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Weight decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.8493
0	60	8 (13.3)	52 (86.7)	NE (NE, NE)	31	3 (9.7)	28 (90.3)	NE (5.2, NE)	0.9899 (0.2540, 3.8585) 0.9884	0.9910	
1	107	18 (16.8)	89 (83.2)	NE (NE, NE)	48	5 (10.4)	43 (89.6)	NE (NE, NE)	1.1986 (0.4425, 3.2464) 0.7217	0.7216	
2	114	20 (17.5)	94 (82.5)	NE (NE, NE)	50	3 (6.0)	47 (94.0)	NE (NE, NE)	2.1558 (0.6363, 7.3045) 0.2173	0.2066	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Weight decreased

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	14 (15.6)	76 (84.4)	NE (NE, NE)	43	3 (7.0)	40 (93.0)	NE (7.2, NE)	1.0618 (0.2952, 3.8189) 0.9269	0.9279	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Weight decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.9788
PD	173	26 (15.0)	147 (85.0)	NE (NE, NE)	77	6 (7.8)	71 (92.2)	NE (NE, NE)	1.2279 (0.4986, 3.0239)	0.6551	
PR	48	5 (10.4)	43 (89.6)	NE (NE, NE)	21	1 (4.8)	20 (95.2)	NE (NE, NE)	1.5981 (0.1846, 13.8347)	0.6675	
SD	82	12 (14.6)	70 (85.4)	NE (NE, NE)	54	5 (9.3)	49 (90.7)	NE (7.2, NE)	1.1142 (0.3873, 3.2055)	0.8410	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Weight decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Reported history of CNS metastases											0.1158
Yes	37	7 (18.9)	30 (81.1)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9946	0.1209	
No	334	53 (15.9)	281 (84.1)	NE (NE, NE)	159	14 (8.8)	145 (91.2)	NE (NE, NE)	1.1112 (0.6109, 2.0210) 0.7298	0.7313	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Weight decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.1493
Yes	24	5 (20.8)	19 (79.2)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9955	0.1906	
No	347	55 (15.9)	292 (84.1)	NE (NE, NE)	165	14 (8.5)	151 (91.5)	NE (NE, NE)	1.1460 (0.6315, 2.0797) 0.6540	0.6550	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Weight decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.2458
Normal Function	201	31 (15.4)	170 (84.6)	NE (NE, NE)	80	9 (11.3)	71 (88.8)	NE (7.9, NE)	0.8753 (0.4095, 1.8706) 0.7310	0.7297	
Mild Impairment	123	18 (14.6)	105 (85.4)	NE (NE, NE)	65	3 (4.6)	62 (95.4)	NE (NE, NE)	1.9828 (0.5755, 6.8311) 0.2781	0.2693	
Moderate Impairment	41	11 (26.8)	30 (73.2)	NE (10.3, NE)	23	2 (8.7)	21 (91.3)	NE (NE, NE)	2.5684 (0.5675, 11.6243) 0.2208	0.2041	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Investigations; PT: Weight decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.2670
Normal Function	170	30 (17.6)	140 (82.4)	NE (NE, NE)	88	10 (11.4)	78 (88.6)	NE (NE, NE)	0.9945 (0.4796, 2.0624) 0.9882	0.9877	
Mild Impairment	194	30 (15.5)	164 (84.5)	NE (NE, NE)	82	4 (4.9)	78 (95.1)	NE (7.9, NE)	2.0743 (0.7242, 5.9415) 0.1742	0.1653	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1187
Yes	331	56 (16.9)	275 (83.1)	NE (NE, NE)	146	11 (7.5)	135 (92.5)	NE (NE, NE)	1.5736 (0.8198, 3.0203) 0.1730	0.1697	
No	40	4 (10.0)	36 (90.0)	NE (NE, NE)	26	3 (11.5)	23 (88.5)	NE (5.2, NE)	0.2264 (0.0421, 1.2169) 0.0834	0.0659	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Weight decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.5317
Positive	329	55 (16.7)	274 (83.3)	NE (NE, NE)	152	12 (7.9)	140 (92.1)	NE (NE, NE)	1.3430 (0.7138, 2.5267) 0.3605	0.3593	
Negative	42	5 (11.9)	37 (88.1)	NE (NE, NE)	20	2 (10.0)	18 (90.0)	NE (NE, NE)	1.1019 (0.2127, 5.7074) 0.9079	0.9059	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Weight decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (derived)											0.3966
Positive	331	55 (16.6)	276 (83.4)	NE (NE, NE)	155	12 (7.7)	143 (92.3)	NE (NE, NE)	1.3673 (0.7266, 2.5731) 0.3321	0.3305	
Negative	40	5 (12.5)	35 (87.5)	NE (NE, NE)	17	2 (11.8)	15 (88.2)	NE (3.0, NE)	0.9284 (0.1786, 4.8251) 0.9296	0.9318	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.5386
HER2 IHC 1+	214	137 (64.0)	77 (36.0)	2.8 (1.2, 5.0)	100	59 (59.0)	41 (41.0)	1.4 (0.6, 4.4)	0.9089 (0.6675, 1.2374) 0.5439	0.5338	
HER2 IHC 2+/ISH Negative	157	111 (70.7)	46 (29.3)	1.6 (0.9, 2.9)	72	43 (59.7)	29 (40.3)	1.4 (0.7, 7.7)	1.0452 (0.7322, 1.4920) 0.8076	0.8182	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.2912
1	220	146 (66.4)	74 (33.6)	2.6 (1.3, 3.8)	94	61 (64.9)	33 (35.1)	1.4 (0.6, 2.6)	0.8557 (0.6324, 1.1579) 0.3125	0.2932	
>=2	150	101 (67.3)	49 (32.7)	1.5 (0.8, 5.0)	78	41 (52.6)	37 (47.4)	3.3 (0.7, NE)	1.1129 (0.7709, 1.6066) 0.5680	0.5598	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.4744
Yes	233	154 (66.1)	79 (33.9)	1.4 (0.8, 3.6)	112	67 (59.8)	45 (40.2)	1.4 (0.7, 3.3)	0.9529 (0.7117, 1.2757) 0.7456	0.7227	
No	98	70 (71.4)	28 (28.6)	2.7 (1.4, 7.7)	43	24 (55.8)	19 (44.2)	2.6 (0.5, NE)	1.1142 (0.6991, 1.7757) 0.6494	0.6481	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3806
<65	289	188 (65.1)	101 (34.9)	2.6 (1.4, 4.3)	126	73 (57.9)	53 (42.1)	1.2 (0.6, 4.4)	0.9317 (0.7084, 1.2254) 0.6128	0.5931	
>=65	82	60 (73.2)	22 (26.8)	0.9 (0.7, 2.8)	46	29 (63.0)	17 (37.0)	2.0 (0.7, 4.6)	1.1427 (0.7323, 1.7831) 0.5567	0.5559	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2589
<75	357	237 (66.4)	120 (33.6)	2.2 (1.4, 3.8)	163	97 (59.5)	66 (40.5)	1.4 (0.7, 2.9)	0.9355 (0.7363, 1.1885) 0.5852	0.5689	
>=75	14	11 (78.6)	3 (21.4)	0.9 (0.1, 3.6)	9	5 (55.6)	4 (44.4)	4.6 (0.1, NE)	1.8751 (0.6445, 5.4550) 0.2486	0.2443	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.0780
White	175	114 (65.1)	61 (34.9)	2.7 (1.3, 4.2)	85	55 (64.7)	30 (35.3)	0.7 (0.5, 1.7)	0.7816 (0.5639, 1.0832) 0.1389	0.1343	
Non-White	196	134 (68.4)	62 (31.6)	1.5 (0.8, 3.8)	86	46 (53.5)	40 (46.5)	2.9 (0.8, NE)	1.1962 (0.8530, 1.6774) 0.2991	0.3060	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.2806
Asia	147	96 (65.3)	51 (34.7)	2.9 (1.2, 8.2)	63	31 (49.2)	32 (50.8)	4.4 (0.8, NE)	1.1204 (0.7428, 1.6899) 0.5878	0.5877	
North America	58	43 (74.1)	15 (25.9)	1.3 (0.5, 3.9)	28	15 (53.6)	13 (46.4)	2.0 (0.4, NE)	1.1933 (0.6578, 2.1649) 0.5608	0.5618	
Europe + Israel	166	109 (65.7)	57 (34.3)	2.1 (0.9, 3.5)	81	56 (69.1)	25 (30.9)	0.7 (0.5, 1.7)	0.8158 (0.5896, 1.1288) 0.2192	0.2044	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.1259
0	199	135 (67.8)	64 (32.2)	2.1 (1.2, 3.1)	95	50 (52.6)	45 (47.4)	2.8 (0.8, NE)	1.1583 (0.8354, 1.6061) 0.3781	0.3847	
1	172	113 (65.7)	59 (34.3)	2.5 (0.8, 4.1)	77	52 (67.5)	25 (32.5)	0.7 (0.5, 2.0)	0.7781 (0.5569, 1.0872) 0.1415	0.1329	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1580
0	60	38 (63.3)	22 (36.7)	2.7 (0.6, 8.2)	31	21 (67.7)	10 (32.3)	0.5 (0.1, 3.9)	0.6492 (0.3731, 1.1295) 0.1263	0.1215	
1	107	63 (58.9)	44 (41.1)	7.7 (2.6, 9.3)	48	30 (62.5)	18 (37.5)	1.7 (0.5, 6.3)	0.7598 (0.4898, 1.1786) 0.2201	0.2154	
2	114	82 (71.9)	32 (28.1)	0.8 (0.6, 1.5)	50	28 (56.0)	22 (44.0)	1.7 (0.7, NE)	1.2946 (0.8412, 1.9922) 0.2404	0.2408	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	65 (72.2)	25 (27.8)	1.5 (0.8, 3.4)	43	23 (53.5)	20 (46.5)	4.4 (0.6, NE)	1.2043 (0.7444, 1.9481) 0.4488	0.4548	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.5186
PD	173	103 (59.5)	70 (40.5)	3.4 (1.5, 7.7)	77	45 (58.4)	32 (41.6)	1.4 (0.6, 4.6)	0.7881 (0.5520, 1.1251)	0.1850	
PR	48	34 (70.8)	14 (29.2)	1.4 (0.2, 11.0)	21	12 (57.1)	9 (42.9)	1.7 (0.4, NE)	1.1589 (0.5913, 2.2712)	0.6851	
SD	82	61 (74.4)	21 (25.6)	1.2 (0.5, 2.4)	54	36 (66.7)	18 (33.3)	0.7 (0.3, 3.9)	1.0197 (0.6737, 1.5434)	0.9307	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.9057
Yes	37	21 (56.8)	16 (43.2)	2.7 (0.3, NE)	13	6 (46.2)	7 (53.8)	NE (0.1, NE)	1.1042 (0.4438, 2.7470)	0.8275	
No	334	227 (68.0)	107 (32.0)	2.1 (1.3, 3.5)	159	96 (60.4)	63 (39.6)	1.4 (0.7, 2.9)	0.9586 (0.7530, 1.2203)	0.7172	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.9790
Yes	24	15 (62.5)	9 (37.5)	1.6 (0.1, NE)	7	4 (57.1)	3 (42.9)	0.5 (0.1, NE)	0.9923 (0.3259, 3.0214) 0.9892	0.9822	
No	347	233 (67.1)	114 (32.9)	2.1 (1.3, 3.5)	165	98 (59.4)	67 (40.6)	1.4 (0.7, 3.3)	0.9603 (0.7564, 1.2191) 0.7391	0.7275	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0397
Normal Function	201	127 (63.2)	74 (36.8)	2.8 (1.5, 4.8)	80	52 (65.0)	28 (35.0)	0.7 (0.5, 2.2)	0.7292 (0.5247, 1.0134) 0.0600	0.0561	
Mild Impairment	123	84 (68.3)	39 (31.7)	1.4 (0.7, 4.0)	65	36 (55.4)	29 (44.6)	1.7 (0.5, NE)	1.1077 (0.7460, 1.6448) 0.6120	0.6213	
Moderate Impairment	41	33 (80.5)	8 (19.5)	0.8 (0.3, 3.6)	23	12 (52.2)	11 (47.8)	3.9 (0.5, NE)	1.7085 (0.8813, 3.3121) 0.1128	0.1071	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.6897
Normal Function	170	117 (68.8)	53 (31.2)	1.4 (0.8, 3.5)	88	54 (61.4)	34 (38.6)	1.4 (0.5, 4.4)	1.0333 (0.7465, 1.4303) 0.8435	0.8647	
Mild Impairment	194	128 (66.0)	66 (34.0)	2.6 (1.2, 4.4)	82	47 (57.3)	35 (42.7)	1.4 (0.7, 6.3)	0.9134 (0.6504, 1.2827) 0.6009	0.6027	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.7013
Yes	331	223 (67.4)	108 (32.6)	2.1 (1.2, 3.5)	146	88 (60.3)	58 (39.7)	1.4 (0.7, 3.3)	0.9774 (0.7619, 1.2539) 0.8573	0.8441	
No	40	25 (62.5)	15 (37.5)	2.4 (0.8, 18.6)	26	14 (53.8)	12 (46.2)	1.3 (0.1, NE)	0.8973 (0.4599, 1.7507) 0.7506	0.7730	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.2195
Positive	329	220 (66.9)	109 (33.1)	2.5 (1.4, 3.9)	152	87 (57.2)	65 (42.8)	1.7 (0.7, 4.4)	1.0083 (0.7846, 1.2959)	0.9483	0.9629
Negative	42	28 (66.7)	14 (33.3)	0.9 (0.3, 4.0)	20	15 (75.0)	5 (25.0)	0.4 (0.1, 3.9)	0.6969 (0.3694, 1.3145)	0.2647	0.2629

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.4116
Positive	331	224 (67.7)	107 (32.3)	2.1 (1.3, 3.6)	155	91 (58.7)	64 (41.3)	1.4 (0.7, 2.9)	0.9912 (0.7748, 1.2680)	0.9288	
Negative	40	24 (60.0)	16 (40.0)	1.5 (0.5, NE)	17	11 (64.7)	6 (35.3)	0.5 (0.1, 4.6)	0.7604 (0.3693, 1.5655)	0.4666	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.6804
HER2 IHC 1+	214	57 (26.6)	157 (73.4)	NE (NE, NE)	100	28 (28.0)	72 (72.0)	NE (NE, NE)	0.8278 (0.5241, 1.3076) 0.4179	0.4113	
HER2 IHC 2+/ISH Negative	157	53 (33.8)	104 (66.2)	NE (NE, NE)	72	22 (30.6)	50 (69.4)	NE (7.7, NE)	0.9196 (0.5561, 1.5207) 0.7439	0.7388	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.5047
1	220	65 (29.5)	155 (70.5)	NE (NE, NE)	94	30 (31.9)	64 (68.1)	NE (NE, NE)	0.7944 (0.5134, 1.2292) 0.3014	0.2957	
>=2	150	45 (30.0)	105 (70.0)	NE (NE, NE)	78	20 (25.6)	58 (74.4)	NE (7.7, NE)	0.9940 (0.5827, 1.6956) 0.9825	0.9780	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.3220
Yes	233	75 (32.2)	158 (67.8)	NE (NE, NE)	112	31 (27.7)	81 (72.3)	NE (NE, NE)	1.0287 (0.6739, 1.5704) 0.8955	0.9061	
No	98	22 (22.4)	76 (77.6)	NE (NE, NE)	43	12 (27.9)	31 (72.1)	NE (7.7, NE)	0.6540 (0.3216, 1.3301) 0.2411	0.2374	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8921
<65	289	86 (29.8)	203 (70.2)	NE (NE, NE)	126	37 (29.4)	89 (70.6)	NE (7.7, NE)	0.8762 (0.5934, 1.2937) 0.5061	0.4921	
>=65	82	24 (29.3)	58 (70.7)	NE (NE, NE)	46	13 (28.3)	33 (71.7)	NE (4.6, NE)	0.8741 (0.4421, 1.7284) 0.6989	0.6984	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5213
<75	357	104 (29.1)	253 (70.9)	NE (NE, NE)	163	47 (28.8)	116 (71.2)	NE (NE, NE)	0.8593 (0.6064, 1.2178) 0.3940	0.3866	
>=75	14	6 (42.9)	8 (57.1)	6.2 (0.9, NE)	9	3 (33.3)	6 (66.7)	NE (0.1, NE)	1.4015 (0.3501, 5.6107) 0.6334	0.6407	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.8466
White	175	61 (34.9)	114 (65.1)	NE (12.7, NE)	85	29 (34.1)	56 (65.9)	NE (4.6, NE)	0.8567 (0.5478, 1.3398) 0.4978	0.4905	
Non-White	196	49 (25.0)	147 (75.0)	NE (NE, NE)	86	20 (23.3)	66 (76.7)	NE (NE, NE)	0.9439 (0.5579, 1.5970) 0.8297	0.8261	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.3767
Asia	147	33 (22.4)	114 (77.6)	NE (NE, NE)	63	12 (19.0)	51 (81.0)	NE (7.7, NE)	1.0145 (0.5193, 1.9821) 0.9664	0.9660	
North America	58	35 (60.3)	23 (39.7)	4.2 (0.7, 11.8)	28	13 (46.4)	15 (53.6)	2.0 (0.6, NE)	1.1133 (0.5815, 2.1315) 0.7460	0.7615	
Europe + Israel	166	42 (25.3)	124 (74.7)	NE (NE, NE)	81	25 (30.9)	56 (69.1)	NE (NE, NE)	0.7023 (0.4264, 1.1566) 0.1650	0.1594	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.6899
0	199	62 (31.2)	137 (68.8)	NE (NE, NE)	95	27 (28.4)	68 (71.6)	NE (NE, NE)	0.9568 (0.6066, 1.5093) 0.8496	0.8441	
1	172	48 (27.9)	124 (72.1)	NE (NE, NE)	77	23 (29.9)	54 (70.1)	NE (7.7, NE)	0.7789 (0.4702, 1.2905) 0.3321	0.3278	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1767
0	60	18 (30.0)	42 (70.0)	NE (NE, NE)	31	13 (41.9)	18 (58.1)	NE (0.5, NE)	0.5861 (0.2841, 1.2091) 0.1482	0.1422	
1	107	22 (20.6)	85 (79.4)	NE (NE, NE)	48	14 (29.2)	34 (70.8)	NE (NE, NE)	0.6180 (0.3149, 1.2127) 0.1617	0.1577	
2	114	42 (36.8)	72 (63.2)	NE (12.7, NE)	50	12 (24.0)	38 (76.0)	NE (NE, NE)	1.4129 (0.7397, 2.6987) 0.2952	0.2924	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	28 (31.1)	62 (68.9)	NE (NE, NE)	43	11 (25.6)	32 (74.4)	NE (7.7, NE)	1.0118 (0.4984, 2.0538) 0.9742	0.9756	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.0936
PD	173	44 (25.4)	129 (74.6)	NE (NE, NE)	77	22 (28.6)	55 (71.4)	NE (NE, NE)	0.7090 (0.4224, 1.1900)	0.1921	
PR	48	18 (37.5)	30 (62.5)	16.2 (12.7, NE)	21	3 (14.3)	18 (85.7)	NE (NE, NE)	2.4783 (0.7211, 8.5174)	0.1386	
SD	82	25 (30.5)	57 (69.5)	NE (NE, NE)	54	21 (38.9)	33 (61.1)	NE (2.3, NE)	0.6617 (0.3675, 1.1913)	0.1633	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.8909
Yes	37	8 (21.6)	29 (78.4)	NE (NE, NE)	13	3 (23.1)	10 (76.9)	NE (0.7, NE)	0.8835 (0.2331, 3.3480)	0.8545	
No	334	102 (30.5)	232 (69.5)	NE (NE, NE)	159	47 (29.6)	112 (70.4)	NE (NE, NE)	0.8554 (0.6183, 1.2442)	0.8771	0.4552

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.4179
Yes	24	6 (25.0)	18 (75.0)	NE (NE, NE)	7	3 (42.9)	4 (57.1)	NE (0.1, NE)	0.5295 (0.1321, 2.1227) 0.3695	0.3644	
No	347	104 (30.0)	243 (70.0)	NE (NE, NE)	165	47 (28.5)	118 (71.5)	NE (NE, NE)	0.8931 (0.6302, 1.2657) 0.5251	0.5173	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.8980
Normal Function	201	63 (31.3)	138 (68.7)	NE (NE, NE)	80	26 (32.5)	54 (67.5)	NE (7.7, NE)	0.7954 (0.4993, 1.2669) 0.3351	0.3278	
Mild Impairment	123	32 (26.0)	91 (74.0)	NE (NE, NE)	65	17 (26.2)	48 (73.8)	NE (NE, NE)	0.8632 (0.4768, 1.5630) 0.6273	0.6217	
Moderate Impairment	41	14 (34.1)	27 (65.9)	NE (6.4, NE)	23	7 (30.4)	16 (69.6)	NE (2.3, NE)	1.0233 (0.4120, 2.5415) 0.9605	0.9617	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.6326
Normal Function	170	50 (29.4)	120 (70.6)	NE (NE, NE)	88	28 (31.8)	60 (68.2)	NE (7.7, NE)	0.7885 (0.4928, 1.2616) 0.3217	0.3110	
Mild Impairment	194	58 (29.9)	136 (70.1)	NE (NE, NE)	82	22 (26.8)	60 (73.2)	NE (NE, NE)	0.9444 (0.5759, 1.5487) 0.8208	0.8193	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1291
Yes	331	100 (30.2)	231 (69.8)	NE (NE, NE)	146	40 (27.4)	106 (72.6)	NE (NE, NE)	0.9665 (0.6677, 1.3990) 0.8566	0.8501	
No	40	10 (25.0)	30 (75.0)	NE (NE, NE)	26	10 (38.5)	16 (61.5)	NE (0.7, NE)	0.4662 (0.1889, 1.1503) 0.0977	0.0917	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.1749
Positive	329	94 (28.6)	235 (71.4)	NE (NE, NE)	152	39 (25.7)	113 (74.3)	NE (NE, NE)	0.9648 (0.6617, 1.4068)	0.8457	
Negative	42	16 (38.1)	26 (61.9)	NE (4.0, NE)	20	11 (55.0)	9 (45.0)	2.6 (0.2, NE)	0.5146 (0.2347, 1.1282)	0.0896	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.5957
Positive	331	96 (29.0)	235 (71.0)	NE (NE, NE)	155	43 (27.7)	112 (72.3)	NE (NE, NE)	0.8980 (0.6243, 1.2915)	0.5541	
Negative	40	14 (35.0)	26 (65.0)	NE (6.0, NE)	17	7 (41.2)	10 (58.8)	4.6 (0.3, NE)	0.5616 (0.2689, 1.7166)	0.4055	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Asthenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0021
HER2 IHC 1+	214	37 (17.3)	177 (82.7)	NE (NE, NE)	100	21 (21.0)	79 (79.0)	NE (NE, NE)	0.6751 (0.3914, 1.1646) 0.1579	0.1537	
HER2 IHC 2+/ISH Negative	157	33 (21.0)	124 (79.0)	NE (NE, NE)	72	4 (5.6)	68 (94.4)	NE (NE, NE)	3.7048 (1.3089, 10.4859) 0.0136	0.0082	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Asthenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.9859
1	220	42 (19.1)	178 (80.9)	NE (NE, NE)	94	14 (14.9)	80 (85.1)	NE (NE, NE)	1.1993 (0.6534, 2.2013) 0.5575	0.5628	
>=2	150	28 (18.7)	122 (81.3)	NE (NE, NE)	78	11 (14.1)	67 (85.9)	NE (NE, NE)	1.1059 (0.5425, 2.2544) 0.7818	0.7865	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Asthenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.4238
Yes	233	49 (21.0)	184 (79.0)	NE (NE, NE)	112	19 (17.0)	93 (83.0)	NE (NE, NE)	1.1349 (0.6651, 1.9367) 0.6425	0.6543	
No	98	18 (18.4)	80 (81.6)	NE (NE, NE)	43	4 (9.3)	39 (90.7)	NE (NE, NE)	1.8274 (0.6139, 5.4395) 0.2787	0.2724	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Asthenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8146
<65	289	54 (18.7)	235 (81.3)	NE (NE, NE)	126	17 (13.5)	109 (86.5)	NE (NE, NE)	1.2264 (0.7072, 2.1270) 0.4675	0.4726	
>=65	82	16 (19.5)	66 (80.5)	NE (NE, NE)	46	8 (17.4)	38 (82.6)	NE (NE, NE)	1.0619 (0.4512, 2.4989) 0.8907	0.8927	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Asthenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1641
<75	357	68 (19.0)	289 (81.0)	NE (NE, NE)	163	25 (15.3)	138 (84.7)	NE (NE, NE)	1.0960 (0.6894, 1.7423) 0.6984	0.7067	
>=75	14	2 (14.3)	12 (85.7)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9978	0.2382	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Asthenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.2687
White	175	38 (21.7)	137 (78.3)	NE (NE, NE)	85	17 (20.0)	68 (80.0)	NE (NE, NE)	0.9421 (0.5288, 1.6783) 0.8396	0.8329	
Non-White	196	32 (16.3)	164 (83.7)	NE (NE, NE)	86	8 (9.3)	78 (90.7)	NE (NE, NE)	1.6433 (0.7528, 3.5873) 0.2124	0.2099	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Asthenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.0941
Asia	147	13 (8.8)	134 (91.2)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (NE, NE)	4.4172 (0.5693, 34.2700) 0.1553	0.1203	
North America	58	3 (5.2)	55 (94.8)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9968	0.3458	
Europe + Israel	166	54 (32.5)	112 (67.5)	NE (NE, NE)	81	24 (29.6)	57 (70.4)	NE (NE, NE)	1.0654 (0.6572, 1.7271) 0.7973	0.8181	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Asthenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.7438
0	199	28 (14.1)	171 (85.9)	NE (NE, NE)	95	9 (9.5)	86 (90.5)	NE (NE, NE)	1.3757 (0.6482, 2.9198) 0.4061	0.4065	
1	172	42 (24.4)	130 (75.6)	NE (18.3, NE)	77	16 (20.8)	61 (79.2)	NE (NE, NE)	1.0135 (0.5634, 1.8231) 0.9643	0.9739	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Asthenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.3634
0	60	7 (11.7)	53 (88.3)	NE (NE, NE)	31	3 (9.7)	28 (90.3)	NE (NE, NE)	1.1365 (0.2930, 4.4080) 0.8532	0.8549	
1	107	20 (18.7)	87 (81.3)	NE (NE, NE)	48	8 (16.7)	40 (83.3)	NE (NE, NE)	1.1486 (0.5054, 2.6105) 0.7409	0.7485	
2	114	24 (21.1)	90 (78.9)	NE (NE, NE)	50	11 (22.0)	39 (78.0)	NE (NE, NE)	0.7791 (0.3762, 1.6132) 0.5014	0.4973	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Asthenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	19 (21.1)	71 (78.9)	NE (18.9, NE)	43	3 (7.0)	40 (93.0)	NE (NE, NE)	2.5758 (0.7541, 8.7988) 0.1311	0.1171	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Asthenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.6330
PD	173	32 (18.5)	141 (81.5)	NE (NE, NE)	77	12 (15.6)	65 (84.4)	NE (NE, NE)	1.0909 (0.5599, 2.1257) 0.7982	0.8053	
PR	48	12 (25.0)	36 (75.0)	18.9 (14.2, NE)	21	5 (23.8)	16 (76.2)	NE (2.5, NE)	0.6852 (0.2271, 2.0674) 0.5023	0.4951	
SD	82	14 (17.1)	68 (82.9)	NE (NE, NE)	54	5 (9.3)	49 (90.7)	NE (NE, NE)	1.7873 (0.6411, 4.9833) 0.2670	0.2635	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Asthenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.9579
Yes	37	4 (10.8)	33 (89.2)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	1.3683 (0.1529, 12.2441)	0.7781	
No	334	66 (19.8)	268 (80.2)	NE (NE, NE)	159	24 (15.1)	135 (84.9)	NE (NE, NE)	1.1657 (0.7270, 1.8691)	0.5321	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Asthenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.3424
Yes	24	2 (8.3)	22 (91.7)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9973	0.4401	
No	347	68 (19.6)	279 (80.4)	NE (NE, NE)	165	25 (15.2)	140 (84.8)	NE (NE, NE)	1.1472 (0.7219, 1.8233) 0.5612	0.5693	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Asthenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.1700
Normal Function	201	34 (16.9)	167 (83.1)	NE (NE, NE)	80	15 (18.8)	65 (81.3)	NE (NE, NE)	0.7763 (0.4202, 1.4342) 0.4189	0.4116	
Mild Impairment	123	24 (19.5)	99 (80.5)	NE (18.9, NE)	65	8 (12.3)	57 (87.7)	NE (NE, NE)	1.4330 (0.6374, 3.2216) 0.3841	0.3849	
Moderate Impairment	41	10 (24.4)	31 (75.6)	NE (18.3, NE)	23	2 (8.7)	21 (91.3)	NE (NE, NE)	2.6674 (0.5756, 12.3611) 0.2098	0.1934	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Asthenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.2410
Normal Function	170	35 (20.6)	135 (79.4)	NE (18.9, NE)	88	11 (12.5)	77 (87.5)	NE (NE, NE)	1.5369 (0.7756, 3.0455) 0.2180	0.2173	
Mild Impairment	194	34 (17.5)	160 (82.5)	NE (NE, NE)	82	14 (17.1)	68 (82.9)	NE (NE, NE)	0.8755 (0.4668, 1.6421) 0.6786	0.6737	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Asthenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1656
Yes	331	63 (19.0)	268 (81.0)	NE (NE, NE)	146	24 (16.4)	122 (83.6)	NE (NE, NE)	1.0396 (0.6472, 1.6700) 0.8723	0.8801	
No	40	7 (17.5)	33 (82.5)	NE (18.3, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	3.9390 (0.4740, 32.7346) 0.2045	0.1709	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Asthenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.9409
Positive	329	65 (19.8)	264 (80.2)	NE (NE, NE)	152	23 (15.1)	129 (84.9)	NE (NE, NE)	1.1813 (0.7315, 1.9077)	0.4957	0.5029
Negative	42	5 (11.9)	37 (88.1)	NE (18.3, NE)	20	2 (10.0)	18 (90.0)	NE (3.9, NE)	0.8894 (0.1620, 4.8844)	0.8927	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Asthenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.2486
Positive	331	68 (20.5)	263 (79.5)	NE (NE, NE)	155	23 (14.8)	132 (85.2)	NE (NE, NE)	1.2498 (0.7756, 2.0139)	0.3650	
Negative	40	2 (5.0)	38 (95.0)	NE (NE, NE)	17	2 (11.8)	15 (88.2)	NE (3.9, NE)	0.3338 (0.0461, 2.4152)	0.2545	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Pyrexia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.2254
HER2 IHC 1+	214	23 (10.7)	191 (89.3)	NE (NE, NE)	100	14 (14.0)	86 (86.0)	NE (NE, NE)	0.4610 (0.2288, 0.9287) 0.0302	0.0269	
HER2 IHC 2+/ISH Negative	157	23 (14.6)	134 (85.4)	NE (NE, NE)	72	8 (11.1)	64 (88.9)	NE (11.0, NE)	0.7967 (0.3493, 1.8168) 0.5889	0.5873	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: General disorders and administration site conditions; PT: Pyrexia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.1074
1	220	26 (11.8)	194 (88.2)	NE (NE, NE)	94	16 (17.0)	78 (83.0)	NE (11.0, NE)	0.4332 (0.2275, 0.8249) 0.0109	0.0091	
>=2	150	20 (13.3)	130 (86.7)	NE (NE, NE)	78	6 (7.7)	72 (92.3)	NE (NE, NE)	0.9964 (0.3873, 2.5631) 0.9940	0.9940	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Pyrexia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.6553
Yes	233	25 (10.7)	208 (89.3)	NE (NE, NE)	112	15 (13.4)	97 (86.6)	NE (11.0, NE)	0.4521 (0.2314, 0.8834) 0.0202	0.0176	
No	98	14 (14.3)	84 (85.7)	NE (NE, NE)	43	6 (14.0)	37 (86.0)	NE (NE, NE)	0.6846 (0.2559, 1.8318) 0.4505	0.4480	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: General disorders and administration site conditions; PT: Pyrexia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9603
<65	289	38 (13.1)	251 (86.9)	NE (NE, NE)	126	17 (13.5)	109 (86.5)	NE (11.0, NE)	0.5757 (0.3180, 1.0424) 0.0683	0.0656	
>=65	82	8 (9.8)	74 (90.2)	NE (NE, NE)	46	5 (10.9)	41 (89.1)	NE (NE, NE)	0.5856 (0.1851, 1.8522) 0.3623	0.3589	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Pyrexia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6331
<75	357	44 (12.3)	313 (87.7)	NE (NE, NE)	163	21 (12.9)	142 (87.1)	NE (NE, NE)	0.5659 (0.3294, 0.9721) 0.0392	0.0370	
>=75	14	2 (14.3)	12 (85.7)	NE (7.5, NE)	9	1 (11.1)	8 (88.9)	NE (0.1, NE)	0.9118 (0.0794, 10.4685) 0.9409	0.9408	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Pyrexia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.9268
White	175	22 (12.6)	153 (87.4)	NE (NE, NE)	85	11 (12.9)	74 (87.1)	NE (11.0, NE)	0.5391 (0.2540, 1.1444) 0.1077	0.1032	
Non-White	196	24 (12.2)	172 (87.8)	NE (NE, NE)	86	11 (12.8)	75 (87.2)	NE (NE, NE)	0.6275 (0.2997, 1.3140) 0.2165	0.2143	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Pyrexia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.9077
Asia	147	18 (12.2)	129 (87.8)	NE (NE, NE)	63	8 (12.7)	55 (87.3)	NE (NE, NE)	0.6104 (0.2567, 1.4512) 0.2639	0.2623	
North America	58	5 (8.6)	53 (91.4)	NE (NE, NE)	28	3 (10.7)	25 (89.3)	NE (NE, NE)	0.6740 (0.1605, 2.8297) 0.5899	0.5876	
Europe + Israel	166	23 (13.9)	143 (86.1)	NE (NE, NE)	81	11 (13.6)	70 (86.4)	NE (11.0, NE)	0.5654 (0.2687, 1.1896) 0.1330	0.1286	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Pyrexia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.0798
0	199	30 (15.1)	169 (84.9)	NE (NE, NE)	95	10 (10.5)	85 (89.5)	NE (NE, NE)	0.8591 (0.4118, 1.7924) 0.6857	0.6863	
1	172	16 (9.3)	156 (90.7)	NE (NE, NE)	77	12 (15.6)	65 (84.4)	NE (NE, NE)	0.3761 (0.1715, 0.8246) 0.0146	0.0114	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Pyrexia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.3119
0	60	12 (20.0)	48 (80.0)	18.6 (18.6, NE)	31	4 (12.9)	27 (87.1)	NE (NE, NE)	0.9308 (0.2853, 3.0368) 0.9053	0.9061	
1	107	8 (7.5)	99 (92.5)	NE (NE, NE)	48	9 (18.8)	39 (81.3)	NE (11.0, NE)	0.2606 (0.0981, 0.6926) 0.0070	0.0040	
2	114	19 (16.7)	95 (83.3)	NE (NE, NE)	50	6 (12.0)	44 (88.0)	NE (NE, NE)	0.8430 (0.3273, 2.1713) 0.7236	0.7245	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Pyrexia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	7 (7.8)	83 (92.2)	NE (NE, NE)	43	3 (7.0)	40 (93.0)	NE (NE, NE)	0.6057 (0.1465, 2.5043) 0.4887	0.4874	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Pyrexia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.4164
PD	173	23 (13.3)	150 (86.7)	NE (18.6, NE)	77	9 (11.7)	68 (88.3)	NE (NE, NE)	0.6114 (0.2716, 1.3764)	0.2320	
PR	48	3 (6.3)	45 (93.8)	NE (NE, NE)	21	3 (14.3)	18 (85.7)	NE (NE, NE)	0.3264 (0.0645, 1.6534)	0.1557	
SD	82	15 (18.3)	67 (81.7)	NE (NE, NE)	54	8 (14.8)	46 (85.2)	NE (11.0, NE)	0.8969 (0.3741, 2.1506)	0.8087	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Pyrexia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.3940
Yes	37	6 (16.2)	31 (83.8)	NE (18.1, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	1.0786 (0.1224, 9.5027)	0.9457	0.9456
No	334	40 (12.0)	294 (88.0)	NE (NE, NE)	159	21 (13.2)	138 (86.8)	NE (NE, NE)	0.5495 (0.3172, 0.9517)	0.0326	0.0306

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Pyrexia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0385
Yes	24	6 (25.0)	18 (75.0)	18.1 (10.3, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9960	0.2642	
No	347	40 (11.5)	307 (88.5)	NE (NE, NE)	165	22 (13.3)	143 (86.7)	NE (NE, NE)	0.5210 (0.3032, 0.8954) 0.0183	0.0167	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Pyrexia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0948
Normal Function	201	28 (13.9)	173 (86.1)	NE (NE, NE)	80	12 (15.0)	68 (85.0)	NE (NE, NE)	0.5508 (0.2725, 1.1133) 0.0967	0.0924	
Mild Impairment	123	11 (8.9)	112 (91.1)	NE (18.6, NE)	65	9 (13.8)	56 (86.2)	NE (11.0, NE)	0.3105 (0.1182, 0.8156) 0.0176	0.0128	
Moderate Impairment	41	7 (17.1)	34 (82.9)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	3.2644 (0.3992, 26.6946) 0.2698	0.2412	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: General disorders and administration site conditions; PT: Pyrexia

Subgroup	Nsub	T-DXd (N=371)			Nsub	TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
		No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.8236
Normal Function	170	22 (12.9)	148 (87.1)	NE (NE, NE)	88	11 (12.5)	77 (87.5)	NE (NE, NE)	0.6933 (0.3300, 1.4569) 0.3337	0.3324	
Mild Impairment	194	24 (12.4)	170 (87.6)	NE (18.6, NE)	82	11 (13.4)	71 (86.6)	NE (11.0, NE)	0.4688 (0.2193, 1.0020) 0.0506	0.0461	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Pyrexia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.4720
Yes	331	41 (12.4)	290 (87.6)	NE (NE, NE)	146	18 (12.3)	128 (87.7)	NE (NE, NE)	0.6376 (0.3609, 1.1264) 0.1212	0.1194	
No	40	5 (12.5)	35 (87.5)	NE (18.6, NE)	26	4 (15.4)	22 (84.6)	NE (NE, NE)	0.3406 (0.0726, 1.5987) 0.1722	0.1555	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Pyrexia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.3129
Positive	329	38 (11.6)	291 (88.4)	NE (NE, NE)	152	20 (13.2)	132 (86.8)	NE (NE, NE)	0.5251 (0.2991, 0.9218)	0.0229	
Negative	42	8 (19.0)	34 (81.0)	NE (7.5, NE)	20	2 (10.0)	18 (90.0)	NE (NE, NE)	1.1120 (0.2189, 5.6478)	0.8981	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Pyrexia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.1909
Positive	331	39 (11.8)	292 (88.2)	NE (NE, NE)	155	21 (13.5)	134 (86.5)	NE (NE, NE)	0.5240 (0.3019, 0.9095)	0.0216	0.0198
Negative	40	7 (17.5)	33 (82.5)	NE (NE, NE)	17	1 (5.9)	16 (94.1)	NE (NE, NE)	1.5219 (0.1726, 13.4201)	0.7053	0.7033

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.3010
HER2 IHC 1+	214	106 (49.5)	108 (50.5)	5.7 (2.8, 17.4)	100	57 (57.0)	43 (43.0)	1.9 (1.0, 4.8)	0.6690 (0.4833, 0.9262) 0.0154	0.0150	
HER2 IHC 2+/ISH Negative	157	89 (56.7)	68 (43.3)	5.6 (2.6, 7.6)	72	35 (48.6)	37 (51.4)	4.0 (1.0, NE)	0.8065 (0.5415, 1.2013) 0.2902	0.2874	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.7198
1	220	127 (57.7)	93 (42.3)	3.2 (1.4, 5.7)	94	57 (60.6)	37 (39.4)	1.0 (0.7, 3.3)	0.6977 (0.5095, 0.9556) 0.0249	0.0242	
>=2	150	67 (44.7)	83 (55.3)	9.5 (6.1, NE)	78	35 (44.9)	43 (55.1)	4.2 (2.1, NE)	0.7054 (0.4631, 1.0746) 0.1042	0.1007	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.7555
Yes	233	122 (52.4)	111 (47.6)	4.9 (2.8, 9.0)	112	59 (52.7)	53 (47.3)	2.1 (1.0, 6.9)	0.7110 (0.5189, 0.9741) 0.0337	0.0326	
No	98	52 (53.1)	46 (46.9)	6.9 (1.8, NE)	43	25 (58.1)	18 (41.9)	2.4 (0.7, NE)	0.6705 (0.4138, 1.0867) 0.1047	0.1016	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7324
<65	289	149 (51.6)	140 (48.4)	5.7 (2.8, 16.1)	126	65 (51.6)	61 (48.4)	3.2 (1.0, 6.9)	0.7268 (0.5411, 0.9762) 0.0340	0.0336	
>=65	82	46 (56.1)	36 (43.9)	5.7 (2.8, 9.0)	46	27 (58.7)	19 (41.3)	2.1 (1.0, 4.0)	0.7313 (0.4518, 1.1838) 0.2029	0.1960	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8041
<75	357	189 (52.9)	168 (47.1)	5.7 (3.5, 9.0)	163	86 (52.8)	77 (47.2)	2.9 (1.0, 4.8)	0.7253 (0.5600, 0.9393) 0.0149	0.0145	
>=75	14	6 (42.9)	8 (57.1)	7.6 (0.7, NE)	9	6 (66.7)	3 (33.3)	2.6 (0.4, NE)	0.6333 (0.2030, 1.9755) 0.4313	0.4274	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.8245
White	175	84 (48.0)	91 (52.0)	6.9 (4.9, 18.2)	85	39 (45.9)	46 (54.1)	3.5 (1.0, NE)	0.7253 (0.4935, 1.0660) 0.1021	0.1036	
Non-White	196	111 (56.6)	85 (43.4)	3.4 (1.4, 7.0)	86	53 (61.6)	33 (38.4)	2.1 (0.9, 4.0)	0.7095 (0.5091, 0.9887) 0.0427	0.0406	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.8156
Asia	147	86 (58.5)	61 (41.5)	2.2 (1.3, 6.9)	63	40 (63.5)	23 (36.5)	1.2 (0.7, 4.0)	0.6647 (0.4541, 0.9729) 0.0356	0.0342	
North America	58	31 (53.4)	27 (46.6)	4.9 (1.4, NE)	28	13 (46.4)	15 (53.6)	4.2 (0.5, NE)	0.8040 (0.4165, 1.5521) 0.5157	0.5091	
Europe + Israel	166	78 (47.0)	88 (53.0)	6.9 (5.3, 17.4)	81	39 (48.1)	42 (51.9)	3.3 (1.9, NE)	0.7376 (0.4999, 1.0882) 0.1250	0.1258	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.4593
0	199	111 (55.8)	88 (44.2)	4.9 (2.7, 9.7)	95	54 (56.8)	41 (43.2)	2.6 (1.0, 4.0)	0.6423 (0.4604, 0.8960) 0.0091	0.0087	
1	172	84 (48.8)	88 (51.2)	6.1 (3.2, NE)	77	38 (49.4)	39 (50.6)	2.9 (0.9, NE)	0.8194 (0.5575, 1.2043) 0.3107	0.3049	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.6245
0	60	31 (51.7)	29 (48.3)	6.3 (1.4, NE)	31	15 (48.4)	16 (51.6)	2.9 (0.7, NE)	0.8340 (0.4465, 1.5578) 0.5690	0.5620	
1	107	56 (52.3)	51 (47.7)	4.6 (1.9, NE)	48	25 (52.1)	23 (47.9)	3.3 (1.1, NE)	0.8875 (0.5523, 1.4260) 0.6217	0.6198	
2	114	60 (52.6)	54 (47.4)	4.9 (2.7, 16.0)	50	27 (54.0)	23 (46.0)	2.1 (0.5, NE)	0.6411 (0.4040, 1.0174) 0.0592	0.0569	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	48 (53.3)	42 (46.7)	6.2 (1.4, 17.4)	43	25 (58.1)	18 (41.9)	1.4 (0.9, 6.9)	0.5929 (0.3604, 0.9755) 0.0396	0.0375	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.9478
PD	173	81 (46.8)	92 (53.2)	9.0 (4.6, NE)	77	36 (46.8)	41 (53.2)	4.0 (1.2, NE)	0.7539 (0.5062, 1.1228)	0.1606	
PR	48	30 (62.5)	18 (37.5)	4.2 (1.0, 6.9)	21	14 (66.7)	7 (33.3)	2.6 (0.3, 6.9)	0.6613 (0.3459, 1.2644)	0.2123	
SD	82	44 (53.7)	38 (46.3)	5.3 (1.5, NE)	54	30 (55.6)	24 (44.4)	1.2 (0.7, NE)	0.7216 (0.4511, 1.1542)	0.1709	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.9188
Yes	37	15 (40.5)	22 (59.5)	16.1 (6.3, NE)	13	5 (38.5)	8 (61.5)	4.2 (0.3, NE)	0.6641 (0.2299, 1.9188)	0.4483	
No	334	180 (53.9)	154 (46.1)	4.9 (2.8, 6.9)	159	87 (54.7)	72 (45.3)	2.1 (1.0, 4.0)	0.7363 (0.5685, 0.9537)	0.0197	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.2578
Yes	24	11 (45.8)	13 (54.2)	16.1 (1.0, NE)	7	5 (71.4)	2 (28.6)	0.7 (0.1, 4.2)	0.4074 (0.1352, 1.2281) 0.1107	0.0983	
No	347	184 (53.0)	163 (47.0)	5.6 (3.4, 8.2)	165	87 (52.7)	78 (47.3)	2.6 (1.1, 5.3)	0.7435 (0.5743, 0.9626) 0.0245	0.0236	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.1830
Normal Function	201	113 (56.2)	88 (43.8)	4.4 (2.1, 6.9)	80	40 (50.0)	40 (50.0)	3.3 (1.0, NE)	0.8365 (0.5802, 1.2060) 0.3389	0.3406	
Mild Impairment	123	63 (51.2)	60 (48.8)	5.6 (1.5, NE)	65	34 (52.3)	31 (47.7)	2.9 (0.9, NE)	0.7575 (0.4970, 1.1545) 0.1964	0.1936	
Moderate Impairment	41	18 (43.9)	23 (56.1)	6.9 (4.6, NE)	23	16 (69.6)	7 (30.4)	1.9 (0.6, 3.5)	0.3676 (0.1834, 0.7368) 0.0048	0.0032	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.2501
Normal Function	170	92 (54.1)	78 (45.9)	6.2 (2.8, 10.6)	88	53 (60.2)	35 (39.8)	2.4 (0.9, 4.0)	0.6268 (0.4440, 0.8850) 0.0080	0.0075	
Mild Impairment	194	100 (51.5)	94 (48.5)	4.9 (2.7, 12.7)	82	38 (46.3)	44 (53.7)	3.5 (1.0, NE)	0.8518 (0.5845, 1.2413) 0.4038	0.4019	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1146
Yes	331	172 (52.0)	159 (48.0)	5.7 (3.5, 9.0)	146	82 (56.2)	64 (43.8)	2.1 (1.0, 4.0)	0.6671 (0.5112, 0.8705) 0.0029	0.0027	
No	40	23 (57.5)	17 (42.5)	5.6 (0.7, 10.6)	26	10 (38.5)	16 (61.5)	5.3 (2.4, NE)	1.1850 (0.5523, 2.5425) 0.6630	0.6632	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence  $\geq 10\%$  in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.3597
Positive	329	172 (52.3)	157 (47.7)	5.7 (3.5, 9.7)	152	82 (53.9)	70 (46.1)	2.4 (1.0, 4.2)	0.6978 (0.5347, 0.9107)	0.0077	
Negative	42	23 (54.8)	19 (45.2)	6.9 (0.9, 9.5)	20	10 (50.0)	10 (50.0)	5.3 (0.5, NE)	0.8648 (0.4005, 1.8673)	0.7087	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.4147
Positive	331	174 (52.6)	157 (47.4)	5.7 (3.5, 9.7)	155	84 (54.2)	71 (45.8)	2.4 (1.0, 4.2)	0.7010 (0.5386, 0.9125)	0.0078	
Negative	40	21 (52.5)	19 (47.5)	6.9 (1.2, NE)	17	8 (47.1)	9 (52.9)	5.3 (0.5, NE)	0.8868 (0.3828, 2.0542)	0.7724	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.2938
HER2 IHC 1+	214	81 (37.9)	133 (62.1)	NE (16.0, NE)	100	36 (36.0)	64 (64.0)	NE (NE, NE)	0.9199 (0.6205, 1.3636) 0.6776	0.6806	
HER2 IHC 2+/ISH Negative	157	66 (42.0)	91 (58.0)	NE (5.6, NE)	72	21 (29.2)	51 (70.8)	NE (NE, NE)	1.2589 (0.7694, 2.0600) 0.3594	0.3567	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.4099
1	220	96 (43.6)	124 (56.4)	NE (4.9, NE)	94	37 (39.4)	57 (60.6)	NE (1.2, NE)	0.9309 (0.6366, 1.3613) 0.7120	0.7149	
>=2	150	51 (34.0)	99 (66.0)	NE (NE, NE)	78	20 (25.6)	58 (74.4)	NE (NE, NE)	1.1776 (0.7001, 1.9809) 0.5378	0.5389	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.3218
Yes	233	99 (42.5)	134 (57.5)	16.0 (5.6, NE)	112	36 (32.1)	76 (67.9)	NE (NE, NE)	1.1055 (0.7536, 1.6218) 0.6079	0.6073	
No	98	34 (34.7)	64 (65.3)	NE (NE, NE)	43	16 (37.2)	27 (62.8)	NE (0.9, NE)	0.8177 (0.4512, 1.4820) 0.5071	0.5084	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3654
<65	289	114 (39.4)	175 (60.6)	NE (NE, NE)	126	44 (34.9)	82 (65.1)	NE (NE, NE)	0.9778 (0.6900, 1.3858) 0.8998	0.9038	
>=65	82	33 (40.2)	49 (59.8)	16.0 (4.4, NE)	46	13 (28.3)	33 (71.7)	NE (NE, NE)	1.2671 (0.6650, 2.4143) 0.4717	0.4721	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1669
<75	357	142 (39.8)	215 (60.2)	NE (16.0, NE)	163	56 (34.4)	107 (65.6)	NE (NE, NE)	0.9897 (0.7256, 1.3500) 0.9480	0.9498	
>=75	14	5 (35.7)	9 (64.3)	NE (0.7, NE)	9	1 (11.1)	8 (88.9)	NE (0.4, NE)	3.5850 (0.4185, 30.7116) 0.2440	0.2129	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.9332
White	175	61 (34.9)	114 (65.1)	NE (NE, NE)	85	25 (29.4)	60 (70.6)	NE (NE, NE)	1.0056 (0.6303, 1.6043) 0.9813	0.9689	
Non-White	196	86 (43.9)	110 (56.1)	NE (4.6, NE)	86	32 (37.2)	54 (62.8)	NE (4.2, NE)	1.0431 (0.6943, 1.5671) 0.8390	0.8433	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.8989
Asia	147	67 (45.6)	80 (54.4)	NE (2.8, NE)	63	23 (36.5)	40 (63.5)	NE (1.9, NE)	1.0980 (0.6830, 1.7650) 0.6996	0.7045	
North America	58	21 (36.2)	37 (63.8)	NE (3.5, NE)	28	9 (32.1)	19 (67.9)	NE (1.0, NE)	0.8986 (0.4112, 1.9635) 0.7886	0.7896	
Europe + Israel	166	59 (35.5)	107 (64.5)	NE (16.0, NE)	81	25 (30.9)	56 (69.1)	NE (NE, NE)	1.0202 (0.6378, 1.6318) 0.9335	0.9229	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.8463
0	199	78 (39.2)	121 (60.8)	NE (16.0, NE)	95	29 (30.5)	66 (69.5)	NE (NE, NE)	1.0820 (0.7054, 1.6595) 0.7181	0.7115	
1	172	69 (40.1)	103 (59.9)	NE (5.7, NE)	77	28 (36.4)	49 (63.6)	NE (NE, NE)	1.0015 (0.6447, 1.5555) 0.9948	0.9987	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.7881
0	60	17 (28.3)	43 (71.7)	NE (NE, NE)	31	10 (32.3)	21 (67.7)	NE (1.8, NE)	0.7994 (0.3653, 1.7494) 0.5753	0.5572	
1	107	47 (43.9)	60 (56.1)	NE (3.0, NE)	48	16 (33.3)	32 (66.7)	NE (NE, NE)	1.2054 (0.6834, 2.1264) 0.5188	0.5141	
2	114	45 (39.5)	69 (60.5)	NE (4.4, NE)	50	17 (34.0)	33 (66.0)	NE (NE, NE)	0.9509 (0.5432, 1.6643) 0.8600	0.8598	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	38 (42.2)	52 (57.8)	NE (6.2, NE)	43	14 (32.6)	29 (67.4)	NE (4.2, NE)	1.1402 (0.6151, 2.1134) 0.6770	0.6696	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.9738
PD	173	62 (35.8)	111 (64.2)	NE (16.0, NE)	77	24 (31.2)	53 (68.8)	NE (NE, NE)	0.9942 (0.6191, 1.5963)	0.9791	
PR	48	19 (39.6)	29 (60.4)	NE (4.2, NE)	21	6 (28.6)	15 (71.4)	NE (1.0, NE)	1.0857 (0.4324, 2.7265)	0.8623	
SD	82	34 (41.5)	48 (58.5)	NE (3.5, NE)	54	20 (37.0)	34 (63.0)	NE (1.9, NE)	0.9920 (0.5702, 1.7258)	0.9761	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.1732
Yes	37	7 (18.9)	30 (81.1)	NE (NE, NE)	13	4 (30.8)	9 (69.2)	NE (0.4, NE)	0.4253 (0.1189, 1.5209)	0.1761	
No	334	140 (41.9)	194 (58.1)	NE (6.6, NE)	159	53 (33.3)	106 (66.7)	NE (NE, NE)	1.1207 (0.8164, 1.5384)	0.4774	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.1070
Yes	24	7 (29.2)	17 (70.8)	NE (6.6, NE)	7	4 (57.1)	3 (42.9)	4.2 (0.4, 4.2)	0.3338 (0.0927, 1.2014) 0.0931	0.0780	
No	347	140 (40.3)	207 (59.7)	NE (16.0, NE)	165	53 (32.1)	112 (67.9)	NE (NE, NE)	1.1068 (0.8062, 1.5195) 0.5302	0.5290	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.6358
Normal Function	201	85 (42.3)	116 (57.7)	NE (5.7, NE)	80	27 (33.8)	53 (66.3)	NE (NE, NE)	1.1105 (0.7191, 1.7149) 0.6364	0.6307	
Mild Impairment	123	47 (38.2)	76 (61.8)	NE (5.6, NE)	65	19 (29.2)	46 (70.8)	NE (NE, NE)	1.1382 (0.6668, 1.9430) 0.6351	0.6364	
Moderate Impairment	41	14 (34.1)	27 (65.9)	NE (6.3, NE)	23	9 (39.1)	14 (60.9)	NE (0.8, NE)	0.7042 (0.3045, 1.6286) 0.4124	0.4111	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.3867
Normal Function	170	71 (41.8)	99 (58.2)	NE (6.9, NE)	88	33 (37.5)	55 (62.5)	NE (NE, NE)	0.9231 (0.6097, 1.3974) 0.7051	0.7091	
Mild Impairment	194	74 (38.1)	120 (61.9)	NE (6.6, NE)	82	23 (28.0)	59 (72.0)	NE (NE, NE)	1.2440 (0.7782, 1.9885) 0.3617	0.3621	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1007
Yes	331	130 (39.3)	201 (60.7)	NE (16.0, NE)	146	52 (35.6)	94 (64.4)	NE (NE, NE)	0.9418 (0.6822, 1.3002) 0.7156	0.7177	
No	40	17 (42.5)	23 (57.5)	NE (1.4, NE)	26	5 (19.2)	21 (80.8)	NE (NE, NE)	2.2031 (0.8105, 5.9887) 0.1216	0.1118	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.6077
Positive	329	132 (40.1)	197 (59.9)	NE (16.0, NE)	152	51 (33.6)	101 (66.4)	NE (NE, NE)	1.0086 (0.7294, 1.3947)	0.9546	
Negative	42	15 (35.7)	27 (64.3)	NE (2.3, NE)	20	6 (30.0)	14 (70.0)	NE (1.8, NE)	1.3518 (0.5233, 3.4920)	0.5382	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.7192
Positive	331	133 (40.2)	198 (59.8)	NE (16.0, NE)	155	52 (33.5)	103 (66.5)	NE (NE, NE)	1.0216 (0.7408, 1.4090)	0.8913	
Negative	40	14 (35.0)	26 (65.0)	NE (2.8, NE)	17	5 (29.4)	12 (70.6)	NE (1.8, NE)	1.2577 (0.4509, 3.5081)	0.6712	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysesthesia syndrome

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.2438
HER2 IHC 1+	214	4 (1.9)	210 (98.1)	NE (NE, NE)	100	13 (13.0)	87 (87.0)	NE (NE, NE)	0.0997 (0.0318, 0.3128) 0.0001	<0.0001	
HER2 IHC 2+/ISH Negative	157	1 (0.6)	156 (99.4)	NE (NE, NE)	72	11 (15.3)	61 (84.7)	NE (NE, NE)	0.0356 (0.0046, 0.2762) 0.0014	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysesthesia syndrome

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.4199
1	220	4 (1.8)	216 (98.2)	NE (NE, NE)	94	14 (14.9)	80 (85.1)	NE (NE, NE)	0.0905 (0.0294, 0.2789) <0.0001	<0.0001	
>=2	150	1 (0.7)	149 (99.3)	NE (NE, NE)	78	10 (12.8)	68 (87.2)	NE (NE, NE)	0.0416 (0.0053, 0.3275) 0.0025	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysesthesia syndrome

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.5664
Yes	233	2 (0.9)	231 (99.1)	NE (NE, NE)	112	16 (14.3)	96 (85.7)	NE (NE, NE)	0.0380 (0.0084, 0.1713) <0.0001	<0.0001	
No	98	2 (2.0)	96 (98.0)	NE (NE, NE)	43	8 (18.6)	35 (81.4)	NE (NE, NE)	0.0900 (0.0190, 0.4258) 0.0024	0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysesthesia syndrome

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0357
<65	289	5 (1.7)	284 (98.3)	NE (NE, NE)	126	13 (10.3)	113 (89.7)	NE (NE, NE)	0.1175 (0.0406, 0.3399)	<0.0001	
>=65	82	0	82 (100)	NE (NE, NE)	46	11 (23.9)	35 (76.1)	NE (NE, NE)	0.0000 (0.0000, ) 0.9924	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysesthesia syndrome

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3552
<75	357	5 (1.4)	352 (98.6)	NE (NE, NE)	163	21 (12.9)	142 (87.1)	NE (NE, NE)	0.0778 (0.0288, 0.2102) <0.0001	<0.0001	
>=75	14	0	14 (100)	NE (NE, NE)	9	3 (33.3)	6 (66.7)	NE (0.6, NE)	0.0000 (0.0000, ) 0.9973	0.0268	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.5135
White	175	3 (1.7)	172 (98.3)	NE (NE, NE)	85	11 (12.9)	74 (87.1)	NE (NE, NE)	0.0994 (0.0272, 0.3637) 0.0005	<0.0001	
Non-White	196	2 (1.0)	194 (99.0)	NE (NE, NE)	86	13 (15.1)	73 (84.9)	NE (NE, NE)	0.0496 (0.0110, 0.2245) 0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Region											0.4119
Asia	147	1 (0.7)	146 (99.3)	NE (NE, NE)	63	11 (17.5)	52 (82.5)	NE (6.9, NE)	0.0274 (0.0035, 0.2171) 0.0007	<0.0001	
North America	58	1 (1.7)	57 (98.3)	NE (NE, NE)	28	4 (14.3)	24 (85.7)	NE (NE, NE)	0.0579 (0.0055, 0.6075) 0.0175	0.0027	
Europe + Israel	166	3 (1.8)	163 (98.2)	NE (NE, NE)	81	9 (11.1)	72 (88.9)	NE (NE, NE)	0.1393 (0.0376, 0.5168) 0.0032	0.0006	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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ECOG PS											0.5874
0	199	3 (1.5)	196 (98.5)	NE (NE, NE)	95	17 (17.9)	78 (82.1)	NE (NE, NE)	0.0518 (0.0148, 0.1808) <0.0001	<0.0001	
1	172	2 (1.2)	170 (98.8)	NE (NE, NE)	77	7 (9.1)	70 (90.9)	NE (NE, NE)	0.1236 (0.0257, 0.5954) 0.0091	0.0019	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.0390
0	60	2 (3.3)	58 (96.7)	NE (NE, NE)	31	1 (3.2)	30 (96.8)	NE (NE, NE)	1.0278 (0.0932, 11.3354) 0.9821	0.9821	
1	107	2 (1.9)	105 (98.1)	NE (NE, NE)	48	7 (14.6)	41 (85.4)	NE (NE, NE)	0.1084 (0.0225, 0.5231) 0.0057	0.0008	
2	114	1 (0.9)	113 (99.1)	NE (NE, NE)	50	7 (14.0)	43 (86.0)	NE (NE, NE)	0.0385 (0.0045, 0.3331) 0.0031	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	0	90 (100)	NE (NE, NE)	43	9 (20.9)	34 (79.1)	NE (6.9, NE)	0.0000 (0.0000, ) 0.9933	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.4759
PD	173	3 (1.7)	170 (98.3)	NE (NE, NE)	77	5 (6.5)	72 (93.5)	NE (NE, NE)	0.1956 (0.0453, 0.8451)	0.0158	
PR	48	1 (2.1)	47 (97.9)	NE (NE, NE)	21	3 (14.3)	18 (85.7)	6.9 (6.9, NE)	0.0639 (0.0056, 0.7250)	0.0056	
SD	82	1 (1.2)	81 (98.8)	NE (NE, NE)	54	10 (18.5)	44 (81.5)	NE (NE, NE)	0.0603 (0.0077, 0.4716)	0.0003	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysesthesia syndrome

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											NE
Yes	37	0	37 (100)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE)	NE	
No	334	5 (1.5)	329 (98.5)	NE (NE, NE)	159	24 (15.1)	135 (84.9)	NE (NE, NE)	0.0728 (0.0273, 0.1938)	<0.0001	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysesthesia syndrome

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											NE
Yes	24	0	24 (100)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE)		
No	347	5 (1.4)	342 (98.6)	NE (NE, NE)	165	24 (14.5)	141 (85.5)	NE (NE, NE)	0.0719 (0.0270, 0.1916) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysesthesia syndrome

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.9157
Normal Function	201	2 (1.0)	199 (99.0)	NE (NE, NE)	80	7 (8.8)	73 (91.3)	NE (NE, NE)	0.0778 (0.0155, 0.3914) 0.0019	<0.0001	
Mild Impairment	123	2 (1.6)	121 (98.4)	NE (NE, NE)	65	9 (13.8)	56 (86.2)	NE (NE, NE)	0.1054 (0.0227, 0.4887) 0.0040	0.0004	
Moderate Impairment	41	1 (2.4)	40 (97.6)	NE (NE, NE)	23	8 (34.8)	15 (65.2)	NE (2.1, NE)	0.0479 (0.0059, 0.3864) 0.0043	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysesthesia syndrome

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.0356
Normal Function	170	0	170 (100)	NE (NE, NE)	88	11 (12.5)	77 (87.5)	NE (NE, NE)	0.0000 (0.0000, ) 0.9927	<0.0001	
Mild Impairment	194	5 (2.6)	189 (97.4)	NE (NE, NE)	82	13 (15.9)	69 (84.1)	NE (NE, NE)	0.1174 (0.0409, 0.3367) 0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysesthesia syndrome

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.2388
Yes	331	5 (1.5)	326 (98.5)	NE (NE, NE)	146	20 (13.7)	126 (86.3)	NE (NE, NE)	0.0829 (0.0307, 0.2238) <0.0001	<0.0001	
No	40	0	40 (100)	NE (NE, NE)	26	4 (15.4)	22 (84.6)	NE (NE, NE)	0.0000 (0.0000, ) 0.9953	0.0046	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysesthesia syndrome

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.2303
Positive	329	4 (1.2)	325 (98.8)	NE (NE, NE)	152	23 (15.1)	129 (84.9)	NE (NE, NE)	0.0572 (0.0195, 0.1678)	<0.0001	
Negative	42	1 (2.4)	41 (97.6)	NE (NE, NE)	20	1 (5.0)	19 (95.0)	NE (NE, NE)	0.4820 (0.0301, 7.7061)	0.5978	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysesthesia syndrome

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.0523
Positive	331	4 (1.2)	327 (98.8)	NE (NE, NE)	155	24 (15.5)	131 (84.5)	NE (NE, NE)	0.0559 (0.0191, 0.1636)	<0.0001	
Negative	40	1 (2.5)	39 (97.5)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) 0.9978	0.5145	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0980
HER2 IHC 1+	214	112 (52.3)	102 (47.7)	6.9 (4.2, 10.2)	100	32 (32.0)	68 (68.0)	NE (6.5, NE)	1.5357 (1.0336, 2.2816) 0.0337	0.0335	
HER2 IHC 2+/ISH Negative	157	76 (48.4)	81 (51.6)	11.7 (4.2, NE)	72	31 (43.1)	41 (56.9)	7.1 (1.6, NE)	0.9528 (0.6243, 1.4542) 0.8228	0.8196	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.3605
1	220	103 (46.8)	117 (53.2)	8.3 (5.5, NE)	94	35 (37.2)	59 (62.8)	NE (4.5, NE)	1.1254 (0.7645, 1.6566) 0.5493	0.5601	
>=2	150	84 (56.0)	66 (44.0)	5.9 (2.8, 10.2)	78	28 (35.9)	50 (64.1)	NE (6.5, NE)	1.4453 (0.9384, 2.2259) 0.0946	0.0926	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.1951
Yes	233	101 (43.3)	132 (56.7)	13.2 (7.1, NE)	112	36 (32.1)	76 (67.9)	NE (6.5, NE)	1.1463 (0.7796, 1.6856) 0.4875	0.4936	
No	98	65 (66.3)	33 (33.7)	2.9 (1.5, 6.2)	43	17 (39.5)	26 (60.5)	NE (2.0, NE)	1.7611 (1.0314, 3.0072) 0.0382	0.0368	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0564
<65	289	148 (51.2)	141 (48.8)	7.1 (4.2, 13.1)	126	39 (31.0)	87 (69.0)	NE (6.5, NE)	1.5114 (1.0588, 2.1575) 0.0229	0.0225	
>=65	82	40 (48.8)	42 (51.2)	7.8 (4.2, NE)	46	24 (52.2)	22 (47.8)	4.5 (1.0, NE)	0.8071 (0.4847, 1.3439) 0.4100	0.4110	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0189
<75	357	184 (51.5)	173 (48.5)	7.1 (4.3, 11.7)	163	56 (34.4)	107 (65.6)	NE (6.5, NE)	1.3519 (0.9997, 1.8282) 0.0502	0.0507	
>=75	14	4 (28.6)	10 (71.4)	NE (0.5, NE)	9	7 (77.8)	2 (22.2)	1.4 (0.3, 7.1)	0.3440 (0.0992, 1.1929) 0.0926	0.0820	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.4466
White	175	76 (43.4)	99 (56.6)	13.2 (7.1, NE)	85	28 (32.9)	57 (67.1)	NE (4.8, NE)	1.0784 (0.6946, 1.6743) 0.7367	0.7380	
Non-White	196	112 (57.1)	84 (42.9)	4.3 (2.8, 7.2)	86	35 (40.7)	51 (59.3)	7.1 (4.5, NE)	1.3802 (0.9425, 2.0214) 0.0978	0.1008	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.4604
Asia	147	89 (60.5)	58 (39.5)	3.7 (1.5, 6.5)	63	28 (44.4)	35 (55.6)	6.5 (2.0, NE)	1.2981 (0.8464, 1.9911) 0.2319	0.2390	
North America	58	29 (50.0)	29 (50.0)	11.8 (2.8, NE)	28	13 (46.4)	15 (53.6)	2.8 (0.7, NE)	0.8353 (0.4253, 1.6406) 0.6012	0.5979	
Europe + Israel	166	70 (42.2)	96 (57.8)	NE (7.1, NE)	81	22 (27.2)	59 (72.8)	NE (NE, NE)	1.3806 (0.8516, 2.2381) 0.1908	0.1920	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.5527
0	199	88 (44.2)	111 (55.8)	13.1 (7.6, NE)	95	25 (26.3)	70 (73.7)	NE (NE, NE)	1.3639 (0.8703, 2.1374) 0.1758	0.1735	
1	172	100 (58.1)	72 (41.9)	3.9 (1.9, 5.9)	77	38 (49.4)	39 (50.6)	4.5 (1.4, NE)	1.1974 (0.8221, 1.7440) 0.3479	0.3576	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.0285
0	60	37 (61.7)	23 (38.3)	2.1 (0.6, 11.7)	31	18 (58.1)	13 (41.9)	1.4 (0.9, NE)	0.9077 (0.5066, 1.6264) 0.7449	0.7291	
1	107	56 (52.3)	51 (47.7)	6.2 (3.6, NE)	48	20 (41.7)	28 (58.3)	NE (2.2, NE)	1.2304 (0.7371, 2.0538) 0.4278	0.4294	
2	114	55 (48.2)	59 (51.8)	7.6 (4.2, NE)	50	8 (16.0)	42 (84.0)	NE (6.5, NE)	2.9117 (1.3814, 6.1371) 0.0050	0.0033	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	40 (44.4)	50 (55.6)	11.8 (6.5, NE)	43	17 (39.5)	26 (60.5)	7.1 (2.0, NE)	0.8146 (0.4537, 1.4626) 0.4923	0.4905	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.3101
PD	173	83 (48.0)	90 (52.0)	6.9 (4.2, NE)	77	25 (32.5)	52 (67.5)	NE (6.5, NE)	1.3041 (0.8313, 2.0457) 0.2477	0.2474	
PR	48	27 (56.3)	21 (43.8)	7.5 (2.8, 14.5)	21	5 (23.8)	16 (76.2)	NE (NE, NE)	2.0608 (0.7870, 5.3966) 0.1409	0.1337	
SD	82	38 (46.3)	44 (53.7)	12.0 (4.1, NE)	54	23 (42.6)	31 (57.4)	NE (2.3, NE)	1.0329 (0.6124, 1.7422) 0.9033	0.9168	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.9472
Yes	37	20 (54.1)	17 (45.9)	4.1 (0.5, NE)	13	5 (38.5)	8 (61.5)	NE (0.2, NE)	1.3355 (0.4974, 3.5862)	0.5657	
No	334	168 (50.3)	166 (49.7)	7.5 (5.5, 12.0)	159	58 (36.5)	101 (63.5)	NE (6.5, NE)	1.2298 (0.9098, 1.6625)	0.1813	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.6952
Yes	24	14 (58.3)	10 (41.7)	1.5 (0.1, NE)	7	4 (57.1)	3 (42.9)	1.0 (0.1, NE)	1.0369 (0.3397, 3.1657) 0.9492	0.9498	
No	347	174 (50.1)	173 (49.9)	7.6 (5.5, 12.0)	165	59 (35.8)	106 (64.2)	NE (6.5, NE)	1.2428 (0.9223, 1.6748) 0.1532	0.1557	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Renal function at baseline											0.4224
Normal Function	201	105 (52.2)	96 (47.8)	6.3 (4.2, 11.7)	80	28 (35.0)	52 (65.0)	NE (6.5, NE)	1.3080 (0.8580, 1.9941) 0.2120	0.2135	
Mild Impairment	123	62 (50.4)	61 (49.6)	7.2 (3.7, NE)	65	24 (36.9)	41 (63.1)	NE (3.0, NE)	1.2329 (0.7653, 1.9861) 0.3895	0.3971	
Moderate Impairment	41	17 (41.5)	24 (58.5)	NE (2.9, NE)	23	11 (47.8)	12 (52.2)	7.1 (0.6, NE)	0.7845 (0.3669, 1.6775) 0.5313	0.5252	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.6994
Normal Function	170	83 (48.8)	87 (51.2)	11.7 (6.2, 14.5)	88	33 (37.5)	55 (62.5)	NE (4.8, NE)	1.0997 (0.7312, 1.6537) 0.6481	0.6593	
Mild Impairment	194	100 (51.5)	94 (48.5)	6.2 (3.5, 19.6)	82	30 (36.6)	52 (63.4)	NE (3.0, NE)	1.3129 (0.8701, 1.9810) 0.1947	0.1973	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.2527
Yes	331	160 (48.3)	171 (51.7)	8.0 (6.2, 14.5)	146	54 (37.0)	92 (63.0)	NE (6.5, NE)	1.1802 (0.8646, 1.6110) 0.2968	0.3029	
No	40	28 (70.0)	12 (30.0)	2.3 (1.3, 6.5)	26	9 (34.6)	17 (65.4)	NE (2.2, NE)	1.8471 (0.8633, 3.9517) 0.1138	0.1099	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.3106
Positive	329	165 (50.2)	164 (49.8)	7.5 (5.0, 13.1)	152	52 (34.2)	100 (65.8)	NE (7.1, NE)	1.3178 (0.9625, 1.8044) 0.0852	0.0861	
Negative	42	23 (54.8)	19 (45.2)	5.9 (0.5, NE)	20	11 (55.0)	9 (45.0)	2.4 (0.3, NE)	0.9278 (0.4442, 1.9376) 0.8418	0.8308	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.1643
Positive	331	167 (50.5)	164 (49.5)	7.5 (4.8, 12.0)	155	53 (34.2)	102 (65.8)	NE (7.1, NE)	1.3316 (0.9753, 1.8183)	0.0720	
Negative	40	21 (52.5)	19 (47.5)	6.2 (0.3, NE)	17	10 (58.8)	7 (41.2)	1.4 (0.3, NE)	0.8143 (0.3746, 1.7704)	0.5821	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.4023
HER2 IHC 1+	214	68 (31.8)	146 (68.2)	NE (NE, NE)	100	17 (17.0)	83 (83.0)	NE (NE, NE)	1.8200 (1.0672, 3.1037) 0.0279	0.0264	
HER2 IHC 2+/ISH Negative	157	50 (31.8)	107 (68.2)	NE (NE, NE)	72	16 (22.2)	56 (77.8)	NE (NE, NE)	1.3138 (0.7456, 2.3149) 0.3451	0.3465	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.6990
1	220	70 (31.8)	150 (68.2)	NE (NE, NE)	94	17 (18.1)	77 (81.9)	NE (NE, NE)	1.7038 (1.0014, 2.8987) 0.0494	0.0474	
>=2	150	47 (31.3)	103 (68.7)	NE (NE, NE)	78	16 (20.5)	62 (79.5)	NE (NE, NE)	1.4348 (0.8100, 2.5417) 0.2159	0.2163	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.7356
Yes	233	66 (28.3)	167 (71.7)	NE (NE, NE)	112	16 (14.3)	96 (85.7)	NE (NE, NE)	1.7998 (1.0386, 3.1190) 0.0362	0.0333	
No	98	39 (39.8)	59 (60.2)	NE (6.5, NE)	43	11 (25.6)	32 (74.4)	NE (NE, NE)	1.5891 (0.8123, 3.1090) 0.1761	0.1776	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2866
<65	289	92 (31.8)	197 (68.2)	NE (NE, NE)	126	21 (16.7)	105 (83.3)	NE (NE, NE)	1.8029 (1.1189, 2.9050) 0.0155	0.0147	
>=65	82	26 (31.7)	56 (68.3)	NE (NE, NE)	46	12 (26.1)	34 (73.9)	NE (NE, NE)	1.1681 (0.5889, 2.3170) 0.6566	0.6506	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5825
<75	357	114 (31.9)	243 (68.1)	NE (NE, NE)	163	32 (19.6)	131 (80.4)	NE (NE, NE)	1.5252 (1.0281, 2.2628) 0.0359	0.0356	
>=75	14	4 (28.6)	10 (71.4)	NE (0.9, NE)	9	1 (11.1)	8 (88.9)	NE (1.0, NE)	2.9932 (0.3337, 26.8529) 0.3274	0.3036	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.4726
White	175	39 (22.3)	136 (77.7)	NE (NE, NE)	85	13 (15.3)	72 (84.7)	NE (NE, NE)	1.2510 (0.6643, 2.3560) 0.4880	0.4868	
Non-White	196	79 (40.3)	117 (59.7)	NE (7.2, NE)	86	20 (23.3)	66 (76.7)	NE (NE, NE)	1.7631 (1.0773, 2.8855) 0.0241	0.0234	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.7473
Asia	147	65 (44.2)	82 (55.8)	NE (4.3, NE)	63	19 (30.2)	44 (69.8)	NE (6.5, NE)	1.4351 (0.8581, 2.4000) 0.1686	0.1735	
North America	58	9 (15.5)	49 (84.5)	NE (NE, NE)	28	3 (10.7)	25 (89.3)	NE (NE, NE)	1.1821 (0.3122, 4.4763) 0.8055	0.8063	
Europe + Israel	166	44 (26.5)	122 (73.5)	NE (NE, NE)	81	11 (13.6)	70 (86.4)	NE (NE, NE)	1.8625 (0.9589, 3.6174) 0.0663	0.0630	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.5082
0	199	55 (27.6)	144 (72.4)	NE (NE, NE)	95	17 (17.9)	78 (82.1)	NE (NE, NE)	1.3843 (0.8009, 2.3926) 0.2441	0.2421	
1	172	63 (36.6)	109 (63.4)	NE (14.5, NE)	77	16 (20.8)	61 (79.2)	NE (6.5, NE)	1.8017 (1.0381, 3.1267) 0.0363	0.0349	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.0116
0	60	19 (31.7)	41 (68.3)	NE (NE, NE)	31	12 (38.7)	19 (61.3)	NE (1.4, NE)	0.7955 (0.3834, 1.6505) 0.5389	0.5180	
1	107	33 (30.8)	74 (69.2)	NE (NE, NE)	48	10 (20.8)	38 (79.2)	NE (NE, NE)	1.4901 (0.7338, 3.0261) 0.2698	0.2663	
2	114	34 (29.8)	80 (70.2)	NE (NE, NE)	50	2 (4.0)	48 (96.0)	NE (6.5, NE)	6.8328 (1.6361, 28.5363) 0.0084	0.0023	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	32 (35.6)	58 (64.4)	NE (14.5, NE)	43	9 (20.9)	34 (79.1)	NE (NE, NE)	1.5112 (0.7164, 3.1879) 0.2783	0.2750	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.1801
PD	173	48 (27.7)	125 (72.3)	NE (NE, NE)	77	13 (16.9)	64 (83.1)	NE (NE, NE)	1.5114 (0.8163, 2.7982)	0.1872	
PR	48	20 (41.7)	28 (58.3)	14.5 (4.1, NE)	21	2 (9.5)	19 (90.5)	NE (NE, NE)	4.0187 (0.9329, 17.3111)	0.0437	
SD	82	25 (30.5)	57 (69.5)	NE (NE, NE)	54	14 (25.9)	40 (74.1)	NE (NE, NE)	1.1524 (0.5972, 2.2238)	0.6791	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.8229
Yes	37	16 (43.2)	21 (56.8)	13.2 (1.5, NE)	13	3 (23.1)	10 (76.9)	NE (0.8, NE)	1.6962 (0.4886, 5.8886) 0.4054	0.3974	
No	334	102 (30.5)	232 (69.5)	NE (NE, NE)	159	30 (18.9)	129 (81.1)	NE (NE, NE)	1.5347 (1.0194, 2.3105) 0.0402	0.0395	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.6623
Yes	24	12 (50.0)	12 (50.0)	4.9 (0.1, NE)	7	3 (42.9)	4 (57.1)	NE (0.1, NE)	1.2076 (0.3402, 4.2864) 0.7704	0.7670	
No	347	106 (30.5)	241 (69.5)	NE (NE, NE)	165	30 (18.2)	135 (81.8)	NE (NE, NE)	1.5767 (1.0489, 2.3701) 0.0286	0.0278	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.7409
Normal Function	201	61 (30.3)	140 (69.7)	NE (NE, NE)	80	14 (17.5)	66 (82.5)	NE (NE, NE)	1.6469 (0.9184, 2.9532) 0.0941	0.0926	
Mild Impairment	123	44 (35.8)	79 (64.2)	NE (14.5, NE)	65	14 (21.5)	51 (78.5)	NE (NE, NE)	1.5866 (0.8662, 2.9062) 0.1350	0.1346	
Moderate Impairment	41	10 (24.4)	31 (75.6)	NE (NE, NE)	23	5 (21.7)	18 (78.3)	NE (NE, NE)	1.0094 (0.3444, 2.9587) 0.9864	0.9806	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.0529
Normal Function	170	55 (32.4)	115 (67.6)	NE (NE, NE)	88	23 (26.1)	65 (73.9)	NE (NE, NE)	1.1021 (0.6743, 1.8012) 0.6982	0.7117	
Mild Impairment	194	61 (31.4)	133 (68.6)	NE (NE, NE)	82	10 (12.2)	72 (87.8)	NE (NE, NE)	2.5761 (1.3180, 5.0351) 0.0056	0.0041	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.9684
Yes	331	99 (29.9)	232 (70.1)	NE (NE, NE)	146	26 (17.8)	120 (82.2)	NE (NE, NE)	1.6136 (1.0457, 2.4898) 0.0306	0.0296	
No	40	19 (47.5)	21 (52.5)	6.5 (2.3, NE)	26	7 (26.9)	19 (73.1)	NE (2.2, NE)	1.5454 (0.6416, 3.7220) 0.3318	0.3343	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.2358
Positive	329	104 (31.6)	225 (68.4)	NE (NE, NE)	152	26 (17.1)	126 (82.9)	NE (NE, NE)	1.7438 (1.1324, 2.6854)	0.0107	
Negative	42	14 (33.3)	28 (66.7)	NE (6.2, NE)	20	7 (35.0)	13 (65.0)	NE (1.0, NE)	0.9616 (0.3857, 2.3970)	0.9212	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.2436
Positive	331	105 (31.7)	226 (68.3)	NE (NE, NE)	155	27 (17.4)	128 (82.6)	NE (NE, NE)	1.7184 (1.1236, 2.6281) 0.0125	0.0117	
Negative	40	13 (32.5)	27 (67.5)	NE (6.2, NE)	17	6 (35.3)	11 (64.7)	NE (1.0, NE)	0.9298 (0.3505, 2.4664) 0.8838	0.8617	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.4724
HER2 IHC 1+	214	24 (11.2)	190 (88.8)	NE (NE, NE)	100	6 (6.0)	94 (94.0)	NE (NE, NE)	1.3142 (0.5297, 3.2606) 0.5556	0.5546	
HER2 IHC 2+/ISH Negative	157	15 (9.6)	142 (90.4)	NE (NE, NE)	72	6 (8.3)	66 (91.7)	NE (NE, NE)	0.8158 (0.3122, 2.1317) 0.6779	0.6762	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.1528
1	220	22 (10.0)	198 (90.0)	NE (NE, NE)	94	9 (9.6)	85 (90.4)	NE (NE, NE)	0.7072 (0.3211, 1.5575) 0.3897	0.3873	
>=2	150	17 (11.3)	133 (88.7)	NE (NE, NE)	78	3 (3.8)	75 (96.2)	NE (NE, NE)	2.2864 (0.6625, 7.8905) 0.1907	0.1788	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.1796
Yes	233	18 (7.7)	215 (92.3)	NE (NE, NE)	112	8 (7.1)	104 (92.9)	NE (NE, NE)	0.7388 (0.3157, 1.7288) 0.4852	0.4829	
No	98	17 (17.3)	81 (82.7)	NE (NE, NE)	43	3 (7.0)	40 (93.0)	NE (NE, NE)	1.9611 (0.5712, 6.7332) 0.2846	0.2757	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5137
<65	289	30 (10.4)	259 (89.6)	NE (NE, NE)	126	7 (5.6)	119 (94.4)	NE (NE, NE)	1.3180 (0.5718, 3.0382) 0.5170	0.5155	
>=65	82	9 (11.0)	73 (89.0)	NE (NE, NE)	46	5 (10.9)	41 (89.1)	NE (NE, NE)	0.7912 (0.2624, 2.3858) 0.6775	0.6769	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2471
<75	357	38 (10.6)	319 (89.4)	NE (NE, NE)	163	10 (6.1)	153 (93.9)	NE (NE, NE)	1.2060 (0.5946, 2.4457) 0.6037	0.6035	
>=75	14	1 (7.1)	13 (92.9)	NE (NE, NE)	9	2 (22.2)	7 (77.8)	NE (0.6, NE)	0.3215 (0.0290, 3.5599) 0.3550	0.3296	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.8806
White	175	21 (12.0)	154 (88.0)	NE (NE, NE)	85	7 (8.2)	78 (91.8)	NE (NE, NE)	1.1074 (0.4658, 2.6330) 0.8174	0.8190	
Non-White	196	18 (9.2)	178 (90.8)	NE (NE, NE)	86	5 (5.8)	81 (94.2)	NE (NE, NE)	1.0316 (0.3764, 2.8268) 0.9518	0.9513	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.9116
Asia	147	15 (10.2)	132 (89.8)	NE (NE, NE)	63	5 (7.9)	58 (92.1)	NE (NE, NE)	0.7963 (0.2840, 2.2326) 0.6650	0.6647	
North America	58	11 (19.0)	47 (81.0)	NE (NE, NE)	28	3 (10.7)	25 (89.3)	NE (NE, NE)	1.5561 (0.4296, 5.6362) 0.5007	0.4990	
Europe + Israel	166	13 (7.8)	153 (92.2)	NE (NE, NE)	81	4 (4.9)	77 (95.1)	NE (NE, NE)	1.1182 (0.3596, 3.4778) 0.8469	0.8480	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.9897
0	199	17 (8.5)	182 (91.5)	NE (NE, NE)	95	5 (5.3)	90 (94.7)	NE (NE, NE)	1.0351 (0.3758, 2.8514) 0.9468	0.9466	
1	172	22 (12.8)	150 (87.2)	NE (NE, NE)	77	7 (9.1)	70 (90.9)	NE (NE, NE)	1.1277 (0.4761, 2.6710) 0.7848	0.7848	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.7460
0	60	8 (13.3)	52 (86.7)	NE (NE, NE)	31	2 (6.5)	29 (93.5)	NE (5.4, NE)	1.4618 (0.3008, 7.1034) 0.6379	0.6358	
1	107	14 (13.1)	93 (86.9)	NE (NE, NE)	48	5 (10.4)	43 (89.6)	NE (NE, NE)	1.0444 (0.3742, 2.9151) 0.9339	0.9330	
2	114	11 (9.6)	103 (90.4)	NE (NE, NE)	50	2 (4.0)	48 (96.0)	NE (NE, NE)	1.6308 (0.3541, 7.5096) 0.5302	0.5272	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	6 (6.7)	84 (93.3)	NE (NE, NE)	43	3 (7.0)	40 (93.0)	NE (NE, NE)	0.5711 (0.1348, 2.4197) 0.4470	0.4417	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.1934
PD	173	18 (10.4)	155 (89.6)	NE (NE, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	2.9095 (0.6692, 12.6508)	0.1358	
PR	48	4 (8.3)	44 (91.7)	NE (NE, NE)	21	2 (9.5)	19 (90.5)	NE (NE, NE)	0.1544 (0.0932, 3.1373)	0.4878	
SD	82	7 (8.5)	75 (91.5)	NE (NE, NE)	54	5 (9.3)	49 (90.7)	NE (NE, NE)	0.5408 (0.2178, 2.2387)	0.5438	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.3673
Yes	37	2 (5.4)	35 (94.6)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9975	0.4852	
No	334	37 (11.1)	297 (88.9)	NE (NE, NE)	159	12 (7.5)	147 (92.5)	NE (NE, NE)	1.0454 (0.5394, 2.0260) 0.8954	0.8952	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.3533
Yes	24	2 (8.3)	22 (91.7)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9973	0.4511	
No	347	37 (10.7)	310 (89.3)	NE (NE, NE)	165	12 (7.3)	153 (92.7)	NE (NE, NE)	1.0294 (0.5309, 1.9961) 0.9317	0.9321	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.5515
Normal Function	201	25 (12.4)	176 (87.6)	NE (NE, NE)	80	6 (7.5)	74 (92.5)	NE (NE, NE)	1.1957 (0.4841, 2.9534) 0.6984	0.6983	
Mild Impairment	123	7 (5.7)	116 (94.3)	NE (NE, NE)	65	4 (6.2)	61 (93.8)	NE (NE, NE)	0.5595 (0.1576, 1.9867) 0.3691	0.3632	
Moderate Impairment	41	7 (17.1)	34 (82.9)	NE (NE, NE)	23	2 (8.7)	21 (91.3)	NE (NE, NE)	1.8420 (0.3822, 8.8773) 0.4465	0.4394	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.2430
Normal Function	170	18 (10.6)	152 (89.4)	NE (NE, NE)	88	4 (4.5)	84 (95.5)	NE (NE, NE)	1.5349 (0.5106, 4.6141) 0.4454	0.4414	
Mild Impairment	194	21 (10.8)	173 (89.2)	NE (NE, NE)	82	8 (9.8)	74 (90.2)	NE (NE, NE)	0.8113 (0.3556, 1.8510) 0.6193	0.6181	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.8888
Yes	331	34 (10.3)	297 (89.7)	NE (NE, NE)	146	10 (6.8)	136 (93.2)	NE (NE, NE)	1.1292 (0.5536, 2.3031) 0.7383	0.7387	
No	40	5 (12.5)	35 (87.5)	NE (NE, NE)	26	2 (7.7)	24 (92.3)	NE (5.4, NE)	0.7015 (0.1208, 4.0725) 0.6928	0.6916	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.8154
Positive	329	35 (10.6)	294 (89.4)	NE (NE, NE)	152	11 (7.2)	141 (92.8)	NE (NE, NE)	1.0425 (0.5249, 2.0708)	0.9052	
Negative	42	4 (9.5)	38 (90.5)	NE (11.7, NE)	20	1 (5.0)	19 (95.0)	NE (NE, NE)	1.4804 (0.1540, 14.2331)	0.7323	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.8378
Positive	331	36 (10.9)	295 (89.1)	NE (NE, NE)	155	11 (7.1)	144 (92.9)	NE (NE, NE)	1.1021 (0.5561, 2.1841)	0.7812	
Negative	40	3 (7.5)	37 (92.5)	NE (11.7, NE)	17	1 (5.9)	16 (94.1)	NE (NE, NE)	0.8353 (0.0757, 9.2223)	0.8831	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.2126
HER2 IHC 1+	214	110 (51.4)	104 (48.6)	7.6 (5.1, 11.8)	100	42 (42.0)	58 (58.0)	4.4 (2.9, NE)	0.9408 (0.6565, 1.3484) 0.7398	0.7367	
HER2 IHC 2+/ISH Negative	157	69 (43.9)	88 (56.1)	11.8 (7.6, NE)	72	32 (44.4)	40 (55.6)	15.4 (0.9, NE)	0.6522 (0.4253, 1.0001) 0.0500	0.0518	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.3756
1	220	97 (44.1)	123 (55.9)	10.6 (7.6, NE)	94	41 (43.6)	53 (56.4)	7.0 (2.9, NE)	0.7412 (0.5115, 1.0743)	0.1124	
>=2	150	82 (54.7)	68 (45.3)	7.2 (4.1, 11.8)	78	33 (42.3)	45 (57.7)	NE (1.7, NE)	0.9237 (0.6138, 1.3900)	0.7270	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.5127
Yes	233	105 (45.1)	128 (54.9)	11.7 (7.6, 13.8)	112	44 (39.3)	68 (60.7)	15.4 (4.3, NE)	0.8266 (0.5777, 1.1828) 0.2976	0.3051	
No	98	59 (60.2)	39 (39.8)	5.5 (2.8, 8.3)	43	20 (46.5)	23 (53.5)	NE (1.0, NE)	1.0200 (0.6127, 1.6982) 0.9392	0.9470	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9216
<65	289	137 (47.4)	152 (52.6)	10.4 (7.2, 13.1)	126	52 (41.3)	74 (58.7)	15.4 (4.1, NE)	0.8311 (0.6009, 1.1496) 0.2637	0.2695	
>=65	82	42 (51.2)	40 (48.8)	7.6 (4.2, 10.6)	46	22 (47.8)	24 (52.2)	7.0 (0.7, NE)	0.7930 (0.4711, 1.3348) 0.3827	0.3850	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8127
<75	357	172 (48.2)	185 (51.8)	9.0 (7.2, 12.1)	163	69 (42.3)	94 (57.7)	7.0 (4.1, NE)	0.8220 (0.6191, 1.0916) 0.1756	0.1796	
>=75	14	7 (50.0)	7 (50.0)	7.6 (0.7, NE)	9	5 (55.6)	4 (44.4)	2.3 (0.3, NE)	0.6272 (0.1962, 2.0048) 0.4314	0.4383	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.6474
White	175	89 (50.9)	86 (49.1)	7.6 (4.1, 12.0)	85	40 (47.1)	45 (52.9)	4.4 (1.0, NE)	0.7640 (0.5230, 1.1161) 0.1640	0.1709	
Non-White	196	90 (45.9)	106 (54.1)	10.4 (7.4, 13.8)	86	34 (39.5)	52 (60.5)	NE (2.9, NE)	0.8501 (0.5701, 1.2677) 0.4257	0.4224	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.5082
Asia	147	66 (44.9)	81 (55.1)	10.4 (7.6, NE)	63	21 (33.3)	42 (66.7)	NE (3.1, NE)	0.9908 (0.6025, 1.6294) 0.9709	0.9524	
North America	58	24 (41.4)	34 (58.6)	11.8 (5.7, NE)	28	11 (39.3)	17 (60.7)	NE (0.5, NE)	0.6298 (0.2987, 1.3276) 0.2242	0.2306	
Europe + Israel	166	89 (53.6)	77 (46.4)	6.9 (3.4, 11.7)	81	42 (51.9)	39 (48.1)	4.2 (0.9, 15.4)	0.7761 (0.5358, 1.1243) 0.1802	0.1862	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.1067
0	199	97 (48.7)	102 (51.3)	8.3 (6.4, 13.1)	95	35 (36.8)	60 (63.2)	15.4 (4.2, NE)	0.9882 (0.6684, 1.4609) 0.9526	0.9551	
1	172	82 (47.7)	90 (52.3)	10.6 (5.6, 12.5)	77	39 (50.6)	38 (49.4)	4.1 (1.0, NE)	0.6408 (0.4338, 0.9466) 0.0254	0.0258	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1452
0	60	27 (45.0)	33 (55.0)	10.4 (4.9, NE)	31	18 (58.1)	13 (41.9)	1.7 (0.3, NE)	0.4196 (0.2226, 0.7909) 0.0072	0.0062	
1	107	54 (50.5)	53 (49.5)	6.2 (3.0, NE)	48	25 (52.1)	23 (47.9)	4.2 (1.4, NE)	0.7972 (0.4951, 1.2836) 0.3510	0.3512	
2	114	59 (51.8)	55 (48.2)	7.6 (5.6, 12.5)	50	19 (38.0)	31 (62.0)	NE (4.1, NE)	1.0330 (0.6110, 1.7463) 0.9036	0.8999	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	39 (43.3)	51 (56.7)	11.8 (8.6, NE)	43	12 (27.9)	31 (72.1)	NE (5.5, NE)	1.0215 (0.5284, 1.9747) 0.9496	0.9466	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.1037
PD	173	83 (48.0)	90 (52.0)	8.3 (5.5, 13.1)	77	33 (42.9)	44 (57.1)	7.0 (2.0, NE)	0.8338 (0.5541, 1.2549)	0.3866	
PR	48	20 (41.7)	28 (58.3)	10.4 (7.6, NE)	21	11 (52.4)	10 (47.6)	1.0 (0.2, NE)	0.4137 (0.1950, 0.8777)	0.0199	
SD	82	43 (52.4)	39 (47.6)	7.4 (2.8, NE)	54	21 (38.9)	33 (61.1)	15.4 (2.9, NE)	1.1407 (0.6730, 1.9335)	0.6263	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.8553
Yes	37	13 (35.1)	24 (64.9)	NE (8.3, NE)	13	4 (30.8)	9 (69.2)	NE (0.3, NE)	0.8001 (0.2531, 2.5289)	0.7159	
No	334	166 (49.7)	168 (50.3)	8.3 (6.4, 11.8)	159	70 (44.0)	89 (56.0)	7.0 (3.1, NE)	0.7041 (0.6205, 1.0928)	0.8234	0.1785

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.9880
Yes	24	8 (33.3)	16 (66.7)	NE (8.3, NE)	7	2 (28.6)	5 (71.4)	NE (0.2, NE)	0.8692 (0.1788, 4.2250) 0.8621	0.8745	
No	347	171 (49.3)	176 (50.7)	8.3 (6.9, 11.8)	165	72 (43.6)	93 (56.4)	7.0 (3.1, NE)	0.8151 (0.6165, 1.0776) 0.1513	0.1545	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.4247
Normal Function	201	93 (46.3)	108 (53.7)	10.6 (6.9, 13.8)	80	34 (42.5)	46 (57.5)	NE (2.3, NE)	0.7341 (0.4915, 1.0965) 0.1310	0.1320	
Mild Impairment	123	62 (50.4)	61 (49.6)	8.6 (6.2, 12.5)	65	23 (35.4)	42 (64.6)	15.4 (4.3, NE)	1.0626 (0.6546, 1.7249) 0.8058	0.7984	
Moderate Impairment	41	22 (53.7)	19 (46.3)	4.2 (0.7, NE)	23	15 (65.2)	8 (34.8)	1.0 (0.3, 7.0)	0.6641 (0.3438, 1.2829) 0.2231	0.2220	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.9869
Normal Function	170	82 (48.2)	88 (51.8)	11.7 (7.6, 13.1)	88	37 (42.0)	51 (58.0)	NE (2.3, NE)	0.8095 (0.5454, 1.2014) 0.2941	0.2995	
Mild Impairment	194	93 (47.9)	101 (52.1)	7.7 (5.5, 12.0)	82	36 (43.9)	46 (56.1)	5.5 (3.1, NE)	0.7897 (0.5348, 1.1662) 0.2352	0.2387	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.7368
Yes	331	162 (48.9)	169 (51.1)	8.6 (6.4, 11.8)	146	64 (43.8)	82 (56.2)	7.0 (3.1, NE)	0.8228 (0.6139, 1.1029) 0.1920	0.1982	
No	40	17 (42.5)	23 (57.5)	12.2 (5.5, NE)	26	10 (38.5)	16 (61.5)	NE (1.0, NE)	0.6875 (0.3055, 1.5473) 0.3653	0.3542	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.0968
Positive	329	164 (49.8)	165 (50.2)	8.3 (6.4, 11.8)	152	64 (42.1)	88 (57.9)	7.0 (4.1, NE)	0.8852 (0.6608, 1.1857)	0.4202	
Negative	42	15 (35.7)	27 (64.3)	10.6 (7.6, NE)	20	10 (50.0)	10 (50.0)	2.9 (0.3, NE)	0.4134 (0.1461, 0.8458)	0.0154	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.0229
Positive	331	165 (49.8)	166 (50.2)	8.3 (6.2, 11.8)	155	64 (41.3)	91 (58.7)	15.4 (4.2, NE)	0.9061 (0.6766, 1.2134)	0.5161	
Negative	40	14 (35.0)	26 (65.0)	10.6 (7.6, NE)	17	10 (58.8)	7 (41.2)	1.0 (0.3, NE)	0.2474 (0.0979, 0.6251)	0.0016	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0434
HER2 IHC 1+	214	83 (38.8)	131 (61.2)	16.1 (10.4, NE)	100	21 (21.0)	79 (79.0)	NE (NE, NE)	1.5226 (0.9378, 2.4722) 0.0891	0.0893	
HER2 IHC 2+/ISH Negative	157	56 (35.7)	101 (64.3)	24.8 (10.4, NE)	72	24 (33.3)	48 (66.7)	15.4 (15.4, NE)	0.7241 (0.4445, 1.1796) 0.1948	0.1953	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.8388
1	220	77 (35.0)	143 (65.0)	NE (10.6, NE)	94	23 (24.5)	71 (75.5)	15.4 (15.4, NE)	1.1127 (0.6939, 1.7843) 0.6576	0.6662	
>=2	150	62 (41.3)	88 (58.7)	12.2 (8.6, NE)	78	22 (28.2)	56 (71.8)	NE (NE, NE)	1.0791 (0.6578, 1.7700) 0.7631	0.7564	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.7264
Yes	233	78 (33.5)	155 (66.5)	NE (11.8, NE)	112	25 (22.3)	87 (77.7)	15.4 (15.4, NE)	1.0793 (0.6810, 1.7107) 0.7454	0.7487	
No	98	48 (49.0)	50 (51.0)	7.6 (4.2, NE)	43	14 (32.6)	29 (67.4)	NE (2.9, NE)	1.3394 (0.7361, 2.4372) 0.3387	0.3401	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7216
<65	289	106 (36.7)	183 (63.3)	24.8 (11.8, NE)	126	32 (25.4)	94 (74.6)	NE (15.4, NE)	1.0819 (0.7238, 1.6171) 0.7011	0.7061	
>=65	82	33 (40.2)	49 (59.8)	11.7 (7.4, NE)	46	13 (28.3)	33 (71.7)	NE (7.0, NE)	1.1263 (0.5870, 2.1611) 0.7206	0.7234	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7284
<75	357	132 (37.0)	225 (63.0)	24.8 (11.7, NE)	163	41 (25.2)	122 (74.8)	NE (15.4, NE)	1.1197 (0.7844, 1.5983) 0.5335	0.5402	
>=75	14	7 (50.0)	7 (50.0)	7.6 (1.4, 16.1)	9	4 (44.4)	5 (55.6)	NE (0.3, NE)	0.7336 (0.2034, 2.6453) 0.6359	0.6514	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.7842
White	175	64 (36.6)	111 (63.4)	NE (11.8, NE)	85	22 (25.9)	63 (74.1)	15.4 (15.4, NE)	1.0388 (0.6338, 1.7027) 0.8800	0.8769	
Non-White	196	75 (38.3)	121 (61.7)	24.8 (9.0, NE)	86	23 (26.7)	63 (73.3)	NE (7.0, NE)	1.1143 (0.6943, 1.7884) 0.6539	0.6655	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.2481
Asia	147	63 (42.9)	84 (57.1)	10.6 (7.6, NE)	63	16 (25.4)	47 (74.6)	NE (NE, NE)	1.3264 (0.7612, 2.3113) 0.3188	0.3276	
North America	58	18 (31.0)	40 (69.0)	NE (11.8, NE)	28	9 (32.1)	19 (67.9)	NE (0.5, NE)	0.6462 (0.2814, 1.4841) 0.3034	0.3046	
Europe + Israel	166	58 (34.9)	108 (65.1)	NE (11.7, NE)	81	20 (24.7)	61 (75.3)	15.4 (7.0, NE)	1.0941 (0.6531, 1.8326) 0.7327	0.7332	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.2060
0	199	80 (40.2)	119 (59.8)	12.2 (8.6, NE)	95	22 (23.2)	73 (76.8)	NE (15.4, NE)	1.3060 (0.8099, 2.1059)	0.2735	
1	172	59 (34.3)	113 (65.7)	24.8 (11.8, 24.8)	77	23 (29.9)	54 (70.1)	NE (5.5, NE)	0.8960 (0.5484, 1.4639)	0.6608	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1834
0	60	22 (36.7)	38 (63.3)	10.6 (6.6, NE)	31	12 (38.7)	19 (61.3)	2.9 (2.0, NE)	0.6028 (0.2927, 1.2417) 0.1698	0.1647	
1	107	46 (43.0)	61 (57.0)	NE (5.4, NE)	48	18 (37.5)	30 (62.5)	15.4 (4.2, NE)	1.0159 (0.5875, 1.7567) 0.9550	0.9600	
2	114	41 (36.0)	73 (64.0)	NE (11.7, NE)	50	7 (14.0)	43 (86.0)	NE (NE, NE)	2.0911 (0.9289, 4.7075) 0.0748	0.0693	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	30 (33.3)	60 (66.7)	24.8 (11.8, NE)	43	8 (18.6)	35 (81.4)	NE (NE, NE)	1.1068 (0.4953, 2.4736) 0.8046	0.8017	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.1365
PD	173	64 (37.0)	109 (63.0)	NE (8.3, NE)	77	20 (26.0)	57 (74.0)	NE (7.0, NE)	1.1408 (0.6867, 1.8953)	0.6135	
PR	48	15 (31.3)	33 (68.8)	24.8 (9.9, 24.8)	21	7 (33.3)	14 (66.7)	NE (0.7, NE)	0.5098 (0.2024, 1.2845)	0.1489	
SD	82	35 (42.7)	47 (57.3)	11.8 (6.2, NE)	54	11 (20.4)	43 (79.6)	NE (15.4, NE)	1.8322 (0.9243, 3.6319)	0.0820	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.8831
Yes	37	10 (27.0)	27 (73.0)	NE (10.4, NE)	13	2 (15.4)	11 (84.6)	NE (NE, NE)	1.2581 (0.2671, 5.9261)	0.7710	
No	334	129 (38.6)	205 (61.4)	16.1 (10.6, NE)	159	43 (27.0)	116 (73.0)	NE (15.4, NE)	1.0928 (0.7699, 1.5512)	0.6233	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.7080
Yes	24	7 (29.2)	17 (70.8)	NE (8.3, NE)	7	2 (28.6)	5 (71.4)	NE (0.7, NE)	0.8816 (0.1754, 4.4309) 0.8784	0.8783	
No	347	132 (38.0)	215 (62.0)	24.8 (11.7, NE)	165	43 (26.1)	122 (73.9)	NE (15.4, NE)	1.1016 (0.7768, 1.5623) 0.5871	0.5906	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.5736
Normal Function	201	70 (34.8)	131 (65.2)	NE (11.7, NE)	80	18 (22.5)	62 (77.5)	NE (NE, NE)	1.0969 (0.6475, 1.8584) 0.7309	0.7324	
Mild Impairment	123	48 (39.0)	75 (61.0)	24.8 (7.7, 24.8)	65	14 (21.5)	51 (78.5)	15.4 (15.4, NE)	1.3985 (0.7645, 2.5582) 0.2764	0.2757	
Moderate Impairment	41	19 (46.3)	22 (53.7)	16.1 (2.0, NE)	23	11 (47.8)	12 (52.2)	7.0 (1.0, NE)	0.8699 (0.4104, 1.8438) 0.7161	0.7102	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.7572
Normal Function	170	64 (37.6)	106 (62.4)	24.8 (11.7, NE)	88	22 (25.0)	66 (75.0)	NE (NE, NE)	1.1812 (0.7221, 1.9323) 0.5071	0.5092	
Mild Impairment	194	71 (36.6)	123 (63.4)	12.1 (8.3, NE)	82	22 (26.8)	60 (73.2)	15.4 (7.0, NE)	0.9803 (0.6025, 1.5949) 0.9361	0.9351	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.5313
Yes	331	125 (37.8)	206 (62.2)	24.8 (10.4, NE)	146	38 (26.0)	108 (74.0)	NE (15.4, NE)	1.1197 (0.7749, 1.6181) 0.5472	0.5507	
No	40	14 (35.0)	26 (65.0)	NE (6.9, NE)	26	7 (26.9)	19 (73.1)	NE (2.3, NE)	0.9245 (0.3639, 2.3492) 0.8690	0.8582	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.3618
Positive	329	126 (38.3)	203 (61.7)	24.8 (11.7, NE)	152	39 (25.7)	113 (74.3)	NE (15.4, NE)	1.1643 (0.8091, 1.6754)	0.4171	
Negative	42	13 (31.0)	29 (69.0)	12.2 (7.6, NE)	20	6 (30.0)	14 (70.0)	NE (2.0, NE)	0.5381 (0.1885, 1.5363)	0.2415	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.1534
Positive	331	127 (38.4)	204 (61.6)	24.8 (11.7, NE)	155	39 (25.2)	116 (74.8)	NE (15.4, NE)	1.1946 (0.8304, 1.7185)	0.3411	
Negative	40	12 (30.0)	28 (70.0)	12.2 (10.4, NE)	17	6 (35.3)	11 (64.7)	NE (1.0, NE)	0.3914 (0.1318, 1.1622)	0.0812	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.6386
HER2 IHC 1+	214	31 (14.5)	183 (85.5)	NE (NE, NE)	100	21 (21.0)	79 (79.0)	NE (NE, NE)	0.5199 (0.2963, 0.9124) 0.0226	0.0210	
HER2 IHC 2+/ISH Negative	157	18 (11.5)	139 (88.5)	NE (NE, NE)	72	10 (13.9)	62 (86.1)	NE (NE, NE)	0.6734 (0.3082, 1.4712) 0.3213	0.3206	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.3693
1	220	26 (11.8)	194 (88.2)	NE (NE, NE)	94	18 (19.1)	76 (80.9)	NE (NE, NE)	0.4932 (0.2685, 0.9058) 0.0227	0.0208	
>=2	150	23 (15.3)	127 (84.7)	NE (NE, NE)	78	13 (16.7)	65 (83.3)	NE (NE, NE)	0.6994 (0.3509, 1.3939) 0.3096	0.3089	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.6062
Yes	233	31 (13.3)	202 (86.7)	NE (NE, NE)	112	19 (17.0)	93 (83.0)	NE (NE, NE)	0.5963 (0.3332, 1.0670) 0.0816	0.0803	
No	98	16 (16.3)	82 (83.7)	NE (NE, NE)	43	7 (16.3)	36 (83.7)	NE (NE, NE)	0.7944 (0.3250, 1.9417) 0.6137	0.6138	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9349
<65	289	37 (12.8)	252 (87.2)	NE (NE, NE)	126	22 (17.5)	104 (82.5)	NE (NE, NE)	0.5598 (0.3273, 0.9577) 0.0342	0.0328	
>=65	82	12 (14.6)	70 (85.4)	NE (NE, NE)	46	9 (19.6)	37 (80.4)	NE (NE, NE)	0.6218 (0.2614, 1.4794) 0.2827	0.2847	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0262
<75	357	46 (12.9)	311 (87.1)	NE (NE, NE)	163	31 (19.0)	132 (81.0)	NE (NE, NE)	0.5218 (0.3286, 0.8286) 0.0058	0.0053	
>=75	14	3 (21.4)	11 (78.6)	NE (3.4, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9973	0.1603	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Blood and lymphatic system disorders; PT: Neutropenia

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.5511
White	175	34 (19.4)	141 (80.6)	NE (NE, NE)	85	20 (23.5)	65 (76.5)	NE (NE, NE)	0.6376 (0.3652, 1.1132) 0.1135	0.1124	
Non-White	196	15 (7.7)	181 (92.3)	NE (NE, NE)	86	11 (12.8)	75 (87.2)	NE (NE, NE)	0.4494 (0.2021, 0.9995) 0.0499	0.0450	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.5908
Asia	147	5 (3.4)	142 (96.6)	NE (NE, NE)	63	3 (4.8)	60 (95.2)	NE (NE, NE)	0.5614 (0.1281, 2.4602) 0.4438	0.4400	
North America	58	1 (1.7)	57 (98.3)	NE (NE, NE)	28	2 (7.1)	26 (92.9)	NE (NE, NE)	0.0000 (0.0000, ) 0.9968	0.0381	
Europe + Israel	166	43 (25.9)	123 (74.1)	NE (NE, NE)	81	26 (32.1)	55 (67.9)	NE (NE, NE)	0.6159 (0.3770, 1.0064) 0.0530	0.0528	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.0896
0	199	27 (13.6)	172 (86.4)	NE (NE, NE)	95	12 (12.6)	83 (87.4)	NE (NE, NE)	0.8268 (0.4157, 1.6442) 0.5876	0.5902	
1	172	22 (12.8)	150 (87.2)	NE (NE, NE)	77	19 (24.7)	58 (75.3)	NE (NE, NE)	0.4026 (0.2155, 0.7520) 0.0043	0.0033	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.7096
0	60	9 (15.0)	51 (85.0)	NE (NE, NE)	31	8 (25.8)	23 (74.2)	NE (NE, NE)	0.4435 (0.1688, 1.1653) 0.0990	0.0918	
1	107	12 (11.2)	95 (88.8)	NE (NE, NE)	48	10 (20.8)	38 (79.2)	NE (NE, NE)	0.4540 (0.1956, 1.0538) 0.0661	0.0604	
2	114	21 (18.4)	93 (81.6)	NE (NE, NE)	50	10 (20.0)	40 (80.0)	NE (NE, NE)	0.6896 (0.3198, 1.4869) 0.3431	0.3424	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	7 (7.8)	83 (92.2)	NE (NE, NE)	43	3 (7.0)	40 (93.0)	NE (NE, NE)	0.8250 (0.2088, 3.2598) 0.7838	0.7835	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.5443
PD	173	26 (15.0)	147 (85.0)	NE (NE, NE)	77	16 (20.8)	61 (79.2)	NE (NE, NE)	0.5260 (0.2785, 0.9937)	0.0450	
PR	48	6 (12.5)	42 (87.5)	NE (NE, NE)	21	5 (23.8)	16 (76.2)	NE (NE, NE)	0.3777 (0.1136, 1.2553)	0.1019	
SD	82	13 (15.9)	69 (84.1)	NE (NE, NE)	54	9 (16.7)	45 (83.3)	NE (NE, NE)	0.8144 (0.3465, 1.9137)	0.6423	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.9342
Yes	37	4 (10.8)	33 (89.2)	NE (NE, NE)	13	2 (15.4)	11 (84.6)	NE (1.0, NE)	0.6421 (0.1176, 3.5072)	0.6065	
No	334	45 (13.5)	289 (86.5)	NE (NE, NE)	159	29 (18.2)	130 (81.8)	NE (NE, NE)	0.6091 (0.3575, 0.9200)	0.5735	0.0203
									0.0211		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.8565
Yes	24	2 (8.3)	22 (91.7)	NE (NE, NE)	7	1 (14.3)	6 (85.7)	NE (0.3, NE)	0.5343 (0.0484, 5.8986) 0.6089	0.6031	
No	347	47 (13.5)	300 (86.5)	NE (NE, NE)	165	30 (18.2)	135 (81.8)	NE (NE, NE)	0.5777 (0.3632, 0.9187) 0.0204	0.0196	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.7522
Normal Function	201	26 (12.9)	175 (87.1)	NE (NE, NE)	80	16 (20.0)	64 (80.0)	NE (NE, NE)	0.4634 (0.2445, 0.8785) 0.0184	0.0163	
Mild Impairment	123	16 (13.0)	107 (87.0)	NE (NE, NE)	65	11 (16.9)	54 (83.1)	NE (NE, NE)	0.6320 (0.2913, 1.3712) 0.2456	0.2446	
Moderate Impairment	41	7 (17.1)	34 (82.9)	NE (NE, NE)	23	4 (17.4)	19 (82.6)	NE (NE, NE)	0.8350 (0.2439, 2.8578) 0.7739	0.7837	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1226
Normal Function	170	20 (11.8)	150 (88.2)	NE (NE, NE)	88	19 (21.6)	69 (78.4)	NE (NE, NE)	0.4036 (0.2128, 0.7655) 0.0055	0.0043	
Mild Impairment	194	29 (14.9)	165 (85.1)	NE (NE, NE)	82	12 (14.6)	70 (85.4)	NE (NE, NE)	0.8255 (0.4187, 1.6273) 0.5797	0.5802	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.5378
Yes	331	46 (13.9)	285 (86.1)	NE (NE, NE)	146	27 (18.5)	119 (81.5)	NE (NE, NE)	0.5950 (0.3682, 0.9615) 0.0340	0.0333	
No	40	3 (7.5)	37 (92.5)	NE (NE, NE)	26	4 (15.4)	22 (84.6)	NE (NE, NE)	0.2893 (0.0566, 1.4794) 0.1363	0.1158	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.1596
Positive	329	47 (14.3)	282 (85.7)	NE (NE, NE)	152	27 (17.8)	125 (82.2)	NE (NE, NE)	0.6234 (0.3862, 1.0062)	0.0525	
Negative	42	2 (4.8)	40 (95.2)	NE (NE, NE)	20	4 (20.0)	16 (80.0)	NE (NE, NE)	0.2250 (0.0412, 1.2291)	0.0604	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.0427
Positive	331	47 (14.2)	284 (85.8)	NE (NE, NE)	155	26 (16.8)	129 (83.2)	NE (NE, NE)	0.6586 (0.4057, 1.0693)	0.0913	
Negative	40	2 (5.0)	38 (95.0)	NE (NE, NE)	17	5 (29.4)	12 (70.6)	NE (0.9, NE)	0.1550 (0.0300, 0.7996)	0.0107	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.8091
HER2 IHC 1+	214	88 (41.1)	126 (58.9)	15.2 (11.0, NE)	100	28 (28.0)	72 (72.0)	NE (NE, NE)	1.0790 (0.7003, 1.6624) 0.7304	0.7278	
HER2 IHC 2+/ISH Negative	157	67 (42.7)	90 (57.3)	13.8 (8.5, 24.4)	72	22 (30.6)	50 (69.4)	NE (8.3, NE)	0.9564 (0.5851, 1.5634) 0.8590	0.8618	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.3408
1	220	91 (41.4)	129 (58.6)	17.9 (11.0, 24.4)	94	24 (25.5)	70 (74.5)	NE (NE, NE)	1.1947 (0.7573, 1.8848) 0.4444	0.4421	
>=2	150	63 (42.0)	87 (58.0)	14.3 (10.5, 17.1)	78	26 (33.3)	52 (66.7)	8.3 (4.1, NE)	0.8427 (0.5272, 1.3471) 0.4747	0.4712	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.8939
Yes	233	101 (43.3)	132 (56.7)	11.8 (8.5, 17.9)	112	33 (29.5)	79 (70.5)	NE (NE, NE)	1.0280 (0.6885, 1.5349) 0.8925	0.8892	
No	98	34 (34.7)	64 (65.3)	23.3 (15.0, NE)	43	11 (25.6)	32 (74.4)	NE (8.3, NE)	0.9894 (0.4964, 1.9717) 0.9757	0.9760	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2891
<65	289	119 (41.2)	170 (58.8)	15.0 (11.8, 23.3)	126	32 (25.4)	94 (74.6)	NE (8.3, NE)	1.1649 (0.7833, 1.7323) 0.4510	0.4508	
>=65	82	36 (43.9)	46 (56.1)	12.6 (7.0, NE)	46	18 (39.1)	28 (60.9)	NE (2.9, NE)	0.7828 (0.4395, 1.3942) 0.4056	0.4050	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2933
<75	357	148 (41.5)	209 (58.5)	14.7 (11.8, 20.4)	163	48 (29.4)	115 (70.6)	NE (8.3, NE)	0.9843 (0.7060, 1.3723) 0.9256	0.9261	
>=75	14	7 (50.0)	7 (50.0)	6.9 (3.3, NE)	9	2 (22.2)	7 (77.8)	NE (0.0, NE)	2.0900 (0.4332, 10.0847) 0.3586	0.3478	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.1084
White	175	85 (48.6)	90 (51.4)	10.5 (5.0, 17.9)	85	23 (27.1)	62 (72.9)	NE (NE, NE)	1.4081 (0.8838, 2.2434) 0.1499	0.1446	
Non-White	196	70 (35.7)	126 (64.3)	14.7 (12.2, NE)	86	27 (31.4)	59 (68.6)	NE (4.4, NE)	0.7297 (0.4629, 1.1501) 0.1746	0.1723	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.5334
Asia	147	47 (32.0)	100 (68.0)	23.3 (12.6, NE)	63	16 (25.4)	47 (74.6)	NE (8.3, NE)	0.7610 (0.4253, 1.3616) 0.3575	0.3566	
North America	58	39 (67.2)	19 (32.8)	3.3 (1.4, 5.4)	28	13 (46.4)	15 (53.6)	4.4 (1.1, NE)	1.2050 (0.6395, 2.2705) 0.5641	0.5490	
Europe + Israel	166	69 (41.6)	97 (58.4)	12.5 (10.3, 20.4)	81	21 (25.9)	60 (74.1)	NE (NE, NE)	1.2175 (0.7409, 2.0007) 0.4375	0.4356	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.0132
0	199	84 (42.2)	115 (57.8)	14.3 (11.0, 24.4)	95	18 (18.9)	77 (81.1)	NE (NE, NE)	1.5577 (0.9295, 2.6104) 0.0925	0.0896	
1	172	71 (41.3)	101 (58.7)	14.7 (10.5, 20.4)	77	32 (41.6)	45 (58.4)	8.3 (3.4, NE)	0.7077 (0.4620, 1.0841) 0.1121	0.1105	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.5084
0	60	21 (35.0)	39 (65.0)	17.1 (12.4, NE)	31	9 (29.0)	22 (71.0)	NE (3.9, NE)	0.8996 (0.4068, 1.9895) 0.7938	0.7946	
1	107	46 (43.0)	61 (57.0)	15.2 (7.4, NE)	48	13 (27.1)	35 (72.9)	NE (NE, NE)	1.3097 (0.7036, 2.4380) 0.3947	0.3928	
2	114	50 (43.9)	64 (56.1)	12.2 (8.2, NE)	50	13 (26.0)	37 (74.0)	NE (NE, NE)	1.1950 (0.6414, 2.2266) 0.5747	0.5737	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	38 (42.2)	52 (57.8)	12.3 (7.5, NE)	43	15 (34.9)	28 (65.1)	8.3 (2.9, NE)	0.6786 (0.3634, 1.2670) 0.2235	0.2199	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.5645
PD	173	68 (39.3)	105 (60.7)	15.0 (10.5, NE)	77	20 (26.0)	57 (74.0)	NE (NE, NE)	1.0355 (0.6224, 1.7228)	0.8913	
PR	48	17 (35.4)	31 (64.6)	13.8 (11.0, NE)	21	7 (33.3)	14 (66.7)	NE (2.9, NE)	0.4742 (0.1804, 1.2462)	0.1194	
SD	82	31 (37.8)	51 (62.2)	23.3 (10.3, NE)	54	15 (27.8)	39 (72.2)	NE (8.3, NE)	1.1104 (0.5942, 2.0750)	0.7426	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.4299
Yes	37	18 (48.6)	19 (51.4)	7.0 (3.4, 24.4)	13	3 (23.1)	10 (76.9)	NE (2.1, NE)	1.5257 (0.4404, 5.2850)	0.5004	
No	334	137 (41.0)	197 (59.0)	14.3 (11.8, 20.4)	159	47 (29.6)	112 (70.4)	NE (8.3, NE)	0.9755 (0.6959, 1.3675)	0.8882	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.9267
Yes	24	9 (37.5)	15 (62.5)	24.4 (3.4, 24.4)	7	2 (28.6)	5 (71.4)	NE (2.1, NE)	1.1406 (0.2384, 5.4562) 0.8691	0.8670	
No	347	146 (42.1)	201 (57.9)	13.8 (11.7, 17.9)	165	48 (29.1)	117 (70.9)	NE (8.3, NE)	1.0148 (0.7281, 1.4145) 0.9308	0.9277	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.8663
Normal Function	201	81 (40.3)	120 (59.7)	15.0 (11.7, 24.4)	80	21 (26.3)	59 (73.8)	NE (8.3, NE)	1.1078 (0.6793, 1.8065) 0.6816	0.6830	
Mild Impairment	123	52 (42.3)	71 (57.7)	13.8 (8.5, NE)	65	19 (29.2)	46 (70.8)	NE (4.4, NE)	0.9607 (0.5609, 1.6453) 0.8839	0.8890	
Moderate Impairment	41	18 (43.9)	23 (56.1)	14.7 (6.9, NE)	23	9 (39.1)	14 (60.9)	NE (1.9, NE)	0.8912 (0.3988, 1.9918) 0.7790	0.7789	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.8074
Normal Function	170	69 (40.6)	101 (59.4)	14.7 (12.2, NE)	88	27 (30.7)	61 (69.3)	NE (8.3, NE)	0.9816 (0.6249, 1.5419) 0.9359	0.9350	
Mild Impairment	194	82 (42.3)	112 (57.7)	12.5 (10.5, 17.1)	82	23 (28.0)	59 (72.0)	NE (4.4, NE)	0.9845 (0.6136, 1.5797) 0.9485	0.9519	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.5123
Yes	331	138 (41.7)	193 (58.3)	13.8 (11.2, 20.4)	146	41 (28.1)	105 (71.9)	NE (NE, NE)	1.0684 (0.7501, 1.5219) 0.7139	0.7111	
No	40	17 (42.5)	23 (57.5)	14.7 (6.6, NE)	26	9 (34.6)	17 (65.4)	NE (2.9, NE)	0.8372 (0.3559, 1.9697) 0.6840	0.6822	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.5175
Positive	329	133 (40.4)	196 (59.6)	15.2 (11.8, 23.3)	152	44 (28.9)	108 (71.1)	NE (NE, NE)	0.9823 (0.6945, 1.3893)	0.9212	
Negative	42	22 (52.4)	20 (47.6)	7.3 (2.8, 14.7)	20	6 (30.0)	14 (70.0)	NE (2.9, NE)	1.2693 (0.4990, 3.2284)	0.6129	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.8873
Positive	331	136 (41.1)	195 (58.9)	15.0 (11.8, 20.4)	155	44 (28.4)	111 (71.6)	NE (NE, NE)	1.0257 (0.7259, 1.4494)	0.8829	
Negative	40	19 (47.5)	21 (52.5)	12.4 (4.0, NE)	17	6 (35.3)	11 (64.7)	4.1 (2.9, NE)	0.9024 (0.3475, 2.3437)	0.8353	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.8481
HER2 IHC 1+	214	22 (10.3)	192 (89.7)	NE (NE, NE)	100	1 (1.0)	99 (99.0)	NE (NE, NE)	5.8839 (0.7846, 44.1237) 0.0847	0.0508	
HER2 IHC 2+/ISH Negative	157	17 (10.8)	140 (89.2)	NE (NE, NE)	72	1 (1.4)	71 (98.6)	NE (NE, NE)	4.5173 (0.5938, 34.3652) 0.1452	0.1109	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.1070
1	220	21 (9.5)	199 (90.5)	NE (NE, NE)	94	2 (2.1)	92 (97.9)	NE (NE, NE)	2.7303 (0.6317, 11.8004) 0.1786	0.1613	
>=2	150	18 (12.0)	132 (88.0)	NE (NE, NE)	78	0	78 (100)	NE (NE, NE)	NE (NE, NE) 0.9922	0.0265	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.2343
Yes	233	25 (10.7)	208 (89.3)	NE (NE, NE)	112	2 (1.8)	110 (98.2)	NE (NE, NE)	3.4769 (0.8116, 14.8954) 0.0932	0.0743	
No	98	10 (10.2)	88 (89.8)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9941	0.1046	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4725
<65	289	32 (11.1)	257 (88.9)	NE (NE, NE)	126	1 (0.8)	125 (99.2)	NE (NE, NE)	7.3681 (0.9983, 54.3824) 0.0502	0.0219	
>=65	82	7 (8.5)	75 (91.5)	NE (NE, NE)	46	1 (2.2)	45 (97.8)	NE (NE, NE)	2.9543 (0.3603, 24.2223) 0.3129	0.2900	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4805
<75	357	37 (10.4)	320 (89.6)	NE (NE, NE)	163	2 (1.2)	161 (98.8)	NE (NE, NE)	4.7361 (1.1299, 19.8516) 0.0334	0.0192	
>=75	14	2 (14.3)	12 (85.7)	NE (5.0, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9979	0.2892	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.1221
White	175	21 (12.0)	154 (88.0)	NE (NE, NE)	85	2 (2.4)	83 (97.6)	NE (NE, NE)	3.1118 (0.7186, 13.4749) 0.1290	0.1099	
Non-White	196	18 (9.2)	178 (90.8)	NE (NE, NE)	86	0	86 (100)	NE (NE, NE)	NE (NE, NE) 0.9925	0.0380	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.4473
Asia	147	12 (8.2)	135 (91.8)	NE (NE, NE)	63	0	63 (100)	NE (NE, NE)	NE (NE, NE) 0.9940	0.1036	
North America	58	9 (15.5)	49 (84.5)	NE (NE, NE)	28	1 (3.6)	27 (96.4)	NE (NE, NE)	2.6668 (0.3322, 21.4056) 0.3560	0.3376	
Europe + Israel	166	18 (10.8)	148 (89.2)	NE (NE, NE)	81	1 (1.2)	80 (98.8)	NE (NE, NE)	5.2075 (0.6849, 39.5949) 0.1109	0.0760	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.7932
0	199	23 (11.6)	176 (88.4)	NE (NE, NE)	95	1 (1.1)	94 (98.9)	NE (NE, NE)	5.9884 (0.8025, 44.6862) 0.0809	0.0474	
1	172	16 (9.3)	156 (90.7)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	4.3358 (0.5652, 33.2633) 0.1582	0.1242	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.6934
0	60	3 (5.0)	57 (95.0)	NE (NE, NE)	31	0	31 (100)	NE (NE, NE)	NE (NE, NE) 0.9966	0.2907	
1	107	8 (7.5)	99 (92.5)	NE (NE, NE)	48	1 (2.1)	47 (97.9)	NE (NE, NE)	2.9970 (0.3739, 24.0244) 0.3014	0.2775	
2	114	19 (16.7)	95 (83.3)	NE (NE, NE)	50	1 (2.0)	49 (98.0)	NE (NE, NE)	4.3519 (0.5725, 33.0832) 0.1553	0.1216	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	9 (10.0)	81 (90.0)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9930	0.2265	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											1.0000
PD	173	20 (11.6)	153 (88.4)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE) 0.9919	0.0223	
PR	48	3 (6.3)	45 (93.8)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	NE (NE, NE) 0.9964	0.5282	
SD	82	7 (8.5)	75 (91.5)	NE (NE, NE)	54	0	54 (100)	NE (NE, NE)	NE (NE, NE) 0.9943	0.0736	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.4882
Yes	37	6 (16.2)	31 (83.8)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9956	0.2250	
No	334	33 (9.9)	301 (90.1)	NE (NE, NE)	159	2 (1.3)	157 (98.7)	NE (NE, NE)	4.3091 (1.0239, 18.1353) 0.0464	0.0301	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.5511
Yes	24	4 (16.7)	20 (83.3)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9964	0.3182	
No	347	35 (10.1)	312 (89.9)	NE (NE, NE)	165	2 (1.2)	163 (98.8)	NE (NE, NE)	4.5708 (1.0891, 19.1840) 0.0378	0.0228	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.3043
Normal Function	201	22 (10.9)	179 (89.1)	NE (NE, NE)	80	1 (1.3)	79 (98.8)	NE (NE, NE)	4.5970 (0.6095, 34.6699) 0.1389	0.1046	
Mild Impairment	123	13 (10.6)	110 (89.4)	NE (NE, NE)	65	0	65 (100)	NE (NE, NE)	NE (NE, NE) 0.9937	0.0760	
Moderate Impairment	41	3 (7.3)	38 (92.7)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	1.4557 (0.1509, 14.0417) 0.7454	0.7439	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.8596
Normal Function	170	15 (8.8)	155 (91.2)	NE (NE, NE)	88	1 (1.1)	87 (98.9)	NE (NE, NE)	4.7367 (0.6169, 36.3685) 0.1348	0.0997	
Mild Impairment	194	24 (12.4)	170 (87.6)	NE (NE, NE)	82	1 (1.2)	81 (98.8)	NE (NE, NE)	5.2973 (0.7086, 39.5997) 0.1043	0.0696	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1699
Yes	331	35 (10.6)	296 (89.4)	NE (NE, NE)	146	1 (0.7)	145 (99.3)	NE (NE, NE)	8.9870 (1.2248, 65.9404) 0.0308	0.0090	
No	40	4 (10.0)	36 (90.0)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	1.7305 (0.1816, 16.4927) 0.6335	0.6272	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (XRS)											0.5373
Positive	329	35 (10.6)	294 (89.4)	NE (NE, NE)	152	2 (1.3)	150 (98.7)	NE (NE, NE)	4.7009 (1.1224, 19.6892)	0.0198	
Negative	42	4 (9.5)	38 (90.5)	NE (12.4, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) 0.9967	0.3110	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.5711
Positive	331	35 (10.6)	296 (89.4)	NE (NE, NE)	155	2 (1.3)	153 (98.7)	NE (NE, NE)	4.7649 (1.1374, 19.9607)	0.0186	
Negative	40	4 (10.0)	36 (90.0)	NE (12.4, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) 0.9968	0.3363	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.2310
HER2 IHC 1+	214	23 (10.7)	191 (89.3)	NE (NE, NE)	100	7 (7.0)	93 (93.0)	NE (NE, NE)	1.3035 (0.5552, 3.0602) 0.5427	0.5418	
HER2 IHC 2+/ISH Negative	157	15 (9.6)	142 (90.4)	NE (24.4, NE)	72	9 (12.5)	63 (87.5)	NE (NE, NE)	0.5424 (0.2315, 1.2708) 0.1591	0.1532	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.9508
1	220	21 (9.5)	199 (90.5)	NE (24.4, NE)	94	8 (8.5)	86 (91.5)	NE (NE, NE)	0.9290 (0.4073, 2.1193) 0.8611	0.8622	
>=2	150	17 (11.3)	133 (88.7)	NE (NE, NE)	78	8 (10.3)	70 (89.7)	NE (8.3, NE)	0.8138 (0.3450, 1.9196) 0.6379	0.6375	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.1053
Yes	233	26 (11.2)	207 (88.8)	NE (24.4, NE)	112	9 (8.0)	103 (92.0)	NE (NE, NE)	1.0808 (0.4998, 2.3370) 0.8435	0.8409	
No	98	2 (2.0)	96 (98.0)	NE (NE, NE)	43	3 (7.0)	40 (93.0)	NE (NE, NE)	0.2132 (0.0350, 1.2999) 0.0938	0.0660	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4480
<65	289	30 (10.4)	259 (89.6)	NE (24.4, NE)	126	10 (7.9)	116 (92.1)	NE (NE, NE)	1.0306 (0.4979, 2.1334) 0.9353	0.9368	
>=65	82	8 (9.8)	74 (90.2)	NE (NE, NE)	46	6 (13.0)	40 (87.0)	NE (NE, NE)	0.6315 (0.2158, 1.8480) 0.4015	0.3992	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1289
<75	357	36 (10.1)	321 (89.9)	NE (24.4, NE)	163	16 (9.8)	147 (90.2)	NE (NE, NE)	0.7969 (0.4373, 1.4524) 0.4585	0.4576	
>=75	14	2 (14.3)	12 (85.7)	NE (3.3, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9978	0.2335	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.0818
White	175	25 (14.3)	150 (85.7)	24.4 (24.4, NE)	85	7 (8.2)	78 (91.8)	NE (NE, NE)	1.3744 (0.5884, 3.2108) 0.4625	0.4577	
Non-White	196	13 (6.6)	183 (93.4)	NE (NE, NE)	86	9 (10.5)	77 (89.5)	NE (NE, NE)	0.5015 (0.2106, 1.1941) 0.1190	0.1122	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.1507
Asia	147	5 (3.4)	142 (96.6)	NE (NE, NE)	63	5 (7.9)	58 (92.1)	NE (NE, NE)	0.2871 (0.0775, 1.0639) 0.0619	0.0483	
North America	58	15 (25.9)	43 (74.1)	NE (14.3, NE)	28	4 (14.3)	24 (85.7)	NE (NE, NE)	1.4380 (0.4715, 4.3862) 0.5232	0.5169	
Europe + Israel	166	18 (10.8)	148 (89.2)	24.4 (24.4, NE)	81	7 (8.6)	74 (91.4)	NE (NE, NE)	1.0475 (0.4319, 2.5408) 0.9182	0.9202	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.2504
0	199	16 (8.0)	183 (92.0)	NE (24.4, NE)	95	4 (4.2)	91 (95.8)	NE (NE, NE)	1.4416 (0.4744, 4.3808) 0.5190	0.5162	
1	172	22 (12.8)	150 (87.2)	NE (NE, NE)	77	12 (15.6)	65 (84.4)	NE (8.3, NE)	0.6651 (0.3255, 1.3590) 0.2633	0.2598	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.3560
0	60	7 (11.7)	53 (88.3)	NE (NE, NE)	31	5 (16.1)	26 (83.9)	NE (NE, NE)	0.5717 (0.1796, 1.8201) 0.3440	0.3363	
1	107	11 (10.3)	96 (89.7)	NE (NE, NE)	48	2 (4.2)	46 (95.8)	NE (NE, NE)	2.3466 (0.5197, 10.5956) 0.2674	0.2526	
2	114	12 (10.5)	102 (89.5)	NE (NE, NE)	50	4 (8.0)	46 (92.0)	NE (NE, NE)	0.9548 (0.2978, 3.0608) 0.9380	0.9392	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	8 (8.9)	82 (91.1)	NE (24.4, NE)	43	5 (11.6)	38 (88.4)	NE (8.3, NE)	0.4896 (0.1487, 1.6119) 0.2401	0.2295	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.7449
PD	173	16 (9.2)	157 (90.8)	NE (24.4, NE)	77	7 (9.1)	70 (90.9)	NE (NE, NE)	0.7677 (0.3104, 1.8987)	0.5677	
PR	48	4 (8.3)	44 (91.7)	NE (NE, NE)	21	3 (14.3)	18 (85.7)	NE (NE, NE)	0.3819 (0.0764, 1.9081)	0.2204	
SD	82	5 (6.1)	77 (93.9)	NE (NE, NE)	54	5 (9.3)	49 (90.7)	NE (8.3, NE)	0.4807 (0.1348, 1.7146)	0.2495	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.6778
Yes	37	5 (13.5)	32 (86.5)	24.4 (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	1.0557 (0.1160, 9.6105)	0.9572	
No	334	33 (9.9)	301 (90.1)	NE (NE, NE)	159	15 (9.4)	144 (90.6)	NE (NE, NE)	0.8509 (0.4582, 1.5798)	0.6088	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.1350
Yes	24	4 (16.7)	20 (83.3)	24.4 (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9967	0.3620	
No	347	34 (9.8)	313 (90.2)	NE (NE, NE)	165	16 (9.7)	149 (90.3)	NE (NE, NE)	0.8069 (0.4416, 1.4745) 0.4855	0.4855	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.1510
Normal Function	201	18 (9.0)	183 (91.0)	NE (24.4, NE)	80	6 (7.5)	74 (92.5)	NE (NE, NE)	0.8721 (0.3385, 2.2469) 0.7769	0.7771	
Mild Impairment	123	11 (8.9)	112 (91.1)	NE (NE, NE)	65	9 (13.8)	56 (86.2)	NE (NE, NE)	0.4991 (0.2037, 1.2232) 0.1286	0.1236	
Moderate Impairment	41	6 (14.6)	35 (85.4)	NE (14.7, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	3.2628 (0.3925, 27.1228) 0.2738	0.2469	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.8729
Normal Function	170	16 (9.4)	154 (90.6)	NE (NE, NE)	88	8 (9.1)	80 (90.9)	NE (NE, NE)	0.7390 (0.3107, 1.7578) 0.4938	0.4918	
Mild Impairment	194	18 (9.3)	176 (90.7)	NE (24.4, NE)	82	8 (9.8)	74 (90.2)	NE (NE, NE)	0.7649 (0.3281, 1.7834) 0.5350	0.5390	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.6658
Yes	331	35 (10.6)	296 (89.4)	NE (24.4, NE)	146	15 (10.3)	131 (89.7)	NE (NE, NE)	0.8337 (0.4515, 1.5395) 0.5611	0.5611	
No	40	3 (7.5)	37 (92.5)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	0.9170 (0.0813, 10.3474) 0.9441	0.9441	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.8519
Positive	329	28 (8.5)	301 (91.5)	NE (24.4, NE)	152	12 (7.9)	140 (92.1)	NE (NE, NE)	0.8349 (0.4194, 1.6619)	0.6079	
Negative	42	10 (23.8)	32 (76.2)	NE (14.7, NE)	20	4 (20.0)	16 (80.0)	NE (3.9, NE)	0.9973 (0.3054, 3.2569)	0.9964	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.6182
Positive	331	30 (9.1)	301 (90.9)	NE (24.4, NE)	155	12 (7.7)	143 (92.3)	NE (NE, NE)	0.8987 (0.4544, 1.7775)	0.7598	
Negative	40	8 (20.0)	32 (80.0)	NE (NE, NE)	17	4 (23.5)	13 (76.5)	NE (2.9, NE)	0.7311 (0.2178, 2.4549)	0.6076	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0169
HER2 IHC 1+	214	71 (33.2)	143 (66.8)	NE (12.0, NE)	100	46 (46.0)	54 (54.0)	4.1 (2.8, NE)	0.4560 (0.3103, 0.6700) 0.0001	<0.0001	
HER2 IHC 2+/ISH Negative	157	75 (47.8)	82 (52.2)	7.2 (4.9, NE)	72	29 (40.3)	43 (59.7)	6.7 (2.3, NE)	0.9512 (0.6164, 1.4678) 0.8212	0.8195	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.7805
1	220	78 (35.5)	142 (64.5)	NE (12.0, NE)	94	38 (40.4)	56 (59.6)	5.8 (3.5, NE)	0.6257 (0.4213, 0.9291) 0.0201	0.0188	
>=2	150	67 (44.7)	83 (55.3)	11.0 (6.4, NE)	78	37 (47.4)	41 (52.6)	3.8 (2.3, NE)	0.6463 (0.4274, 0.9773) 0.0386	0.0370	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.9415
Yes	233	91 (39.1)	142 (60.9)	12.6 (7.2, NE)	112	50 (44.6)	62 (55.4)	4.1 (2.3, 6.9)	0.5796 (0.4056, 0.8283) 0.0028	0.0024	
No	98	34 (34.7)	64 (65.3)	NE (12.0, NE)	43	18 (41.9)	25 (58.1)	NE (2.8, NE)	0.6289 (0.3521, 1.1231) 0.1170	0.1133	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2361
<65	289	114 (39.4)	175 (60.6)	18.1 (11.0, NE)	126	58 (46.0)	68 (54.0)	4.1 (2.3, NE)	0.5686 (0.4105, 0.7876) 0.0007	0.0006	
>=65	82	32 (39.0)	50 (61.0)	NE (7.2, NE)	46	17 (37.0)	29 (63.0)	6.9 (3.8, NE)	0.8401 (0.4627, 1.5250) 0.5667	0.5634	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2267
<75	357	139 (38.9)	218 (61.1)	18.1 (11.0, NE)	163	71 (43.6)	92 (56.4)	4.5 (2.8, NE)	0.6140 (0.4579, 0.8234) 0.0011	0.0010	
>=75	14	7 (50.0)	7 (50.0)	5.5 (0.1, NE)	9	4 (44.4)	5 (55.6)	5.5 (0.7, NE)	1.2455 (0.3625, 4.2792) 0.7274	0.7269	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.3538
White	175	71 (40.6)	104 (59.4)	11.0 (6.5, NE)	85	42 (49.4)	43 (50.6)	4.1 (2.0, 5.8)	0.5681 (0.3837, 0.8411) 0.0047	0.0041	
Non-White	196	75 (38.3)	121 (61.7)	18.1 (11.6, NE)	86	32 (37.2)	54 (62.8)	NE (3.5, NE)	0.7366 (0.4829, 1.1237) 0.1560	0.1538	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.7575
Asia	147	54 (36.7)	93 (63.3)	NE (11.6, NE)	63	23 (36.5)	40 (63.5)	NE (2.8, NE)	0.7424 (0.4517, 1.2202) 0.2401	0.2376	
North America	58	22 (37.9)	36 (62.1)	12.6 (4.9, NE)	28	14 (50.0)	14 (50.0)	4.3 (1.0, NE)	0.5081 (0.2552, 1.0118) 0.0540	0.0497	
Europe + Israel	166	70 (42.2)	96 (57.8)	11.0 (6.9, NE)	81	38 (46.9)	43 (53.1)	4.5 (2.3, 6.9)	0.6113 (0.4067, 0.9186) 0.0179	0.0167	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.9139
0	199	80 (40.2)	119 (59.8)	18.1 (8.3, NE)	95	41 (43.2)	54 (56.8)	4.5 (2.3, NE)	0.6106 (0.4148, 0.8988) 0.0124	0.0113	
1	172	66 (38.4)	106 (61.6)	NE (8.5, NE)	77	34 (44.2)	43 (55.8)	5.0 (2.8, NE)	0.6615 (0.4332, 1.0100) 0.0556	0.0536	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.6428
0	60	27 (45.0)	33 (55.0)	8.3 (3.8, NE)	31	16 (51.6)	15 (48.4)	2.8 (0.7, NE)	0.5822 (0.3085, 1.0985) 0.0949	0.0907	
1	107	35 (32.7)	72 (67.3)	NE (8.5, NE)	48	23 (47.9)	25 (52.1)	5.5 (2.3, NE)	0.5225 (0.3069, 0.8895) 0.0168	0.0149	
2	114	44 (38.6)	70 (61.4)	NE (6.5, NE)	50	21 (42.0)	29 (58.0)	4.3 (2.3, NE)	0.6415 (0.3760, 1.0946) 0.1034	0.0996	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]		
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	40 (44.4)	50 (55.6)	43	15 (34.9)	28 (65.1)	11.7 (5.5, NE)	5.8 (2.1, NE)	0.8894 (0.4818, 1.6416) 0.7077	0.7052

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.0753
PD	173	67 (38.7)	106 (61.3)	NE (6.5, NE)	77	34 (44.2)	43 (55.8)	4.5 (3.0, NE)	0.6353 (0.4177, 0.9664)	0.0326	
PR	48	24 (50.0)	24 (50.0)	11.0 (2.9, NE)	21	5 (23.8)	16 (76.2)	NE (2.3, NE)	1.8099 (0.6837, 4.7910)	0.2288	
SD	82	32 (39.0)	50 (61.0)	12.6 (7.2, NE)	54	25 (46.3)	29 (53.7)	5.5 (2.1, NE)	0.5568 (0.3246, 0.9552)	0.0313	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.3249
Yes	37	20 (54.1)	17 (45.9)	5.1 (1.0, 12.4)	13	6 (46.2)	7 (53.8)	6.7 (1.2, 6.7)	0.9275 (0.3613, 2.3809) 0.8757	0.8698	
No	334	126 (37.7)	208 (62.3)	NE (11.0, NE)	159	69 (43.4)	90 (56.6)	5.0 (3.0, NE)	0.6049 (0.4478, 0.8170) 0.0010	0.0009	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.1029
Yes	24	15 (62.5)	9 (37.5)	4.5 (0.8, 12.4)	7	3 (42.9)	4 (57.1)	6.7 (2.1, 6.7)	1.5206 (0.4276, 5.4069) 0.5173	0.5246	
No	347	131 (37.8)	216 (62.2)	NE (11.0, NE)	165	72 (43.6)	93 (56.4)	5.0 (3.0, NE)	0.5983 (0.4456, 0.8033) 0.0006	0.0006	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.1722
Normal Function	201	76 (37.8)	125 (62.2)	NE (10.6, NE)	80	38 (47.5)	42 (52.5)	4.1 (2.3, NE)	0.5601 (0.3758, 0.8349) 0.0044	0.0039	
Mild Impairment	123	58 (47.2)	65 (52.8)	9.4 (5.7, 18.1)	65	24 (36.9)	41 (63.1)	NE (2.7, NE)	0.8833 (0.5415, 1.4409) 0.6193	0.6091	
Moderate Impairment	41	12 (29.3)	29 (70.7)	NE (8.5, NE)	23	11 (47.8)	12 (52.2)	6.7 (3.5, NE)	0.4595 (0.2009, 1.0512) 0.0655	0.0598	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.6836
Normal Function	170	69 (40.6)	101 (59.4)	NE (8.2, NE)	88	42 (47.7)	46 (52.3)	4.5 (2.8, NE)	0.6068 (0.4100, 0.8979) 0.0125	0.0114	
Mild Impairment	194	77 (39.7)	117 (60.3)	12.0 (8.5, NE)	82	33 (40.2)	49 (59.8)	5.8 (2.3, NE)	0.6856 (0.4512, 1.0419) 0.0771	0.0749	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.4755
Yes	331	130 (39.3)	201 (60.7)	12.6 (11.0, NE)	146	63 (43.2)	83 (56.8)	5.0 (3.5, NE)	0.6561 (0.4824, 0.8924) 0.0072	0.0067	
No	40	16 (40.0)	24 (60.0)	NE (5.5, NE)	26	12 (46.2)	14 (53.8)	NE (0.2, NE)	0.5418 (0.2474, 1.1865) 0.1254	0.1196	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.2188
Positive	329	123 (37.4)	206 (62.6)	NE (11.6, NE)	152	66 (43.4)	86 (56.6)	4.5 (2.9, NE)	0.5959 (0.4384, 0.8099) 0.0009	0.0008	
Negative	42	23 (54.8)	19 (45.2)	3.8 (2.5, 12.4)	20	9 (45.0)	11 (55.0)	5.0 (0.2, NE)	0.9381 (0.4292, 2.0503) 0.8728	0.8760	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.2189
Positive	331	125 (37.8)	206 (62.2)	NE (11.6, NE)	155	68 (43.9)	87 (56.1)	4.5 (2.9, NE)	0.5969 (0.4409, 0.8080)	0.0007	
Negative	40	21 (52.5)	19 (47.5)	4.2 (2.5, 12.4)	17	7 (41.2)	10 (58.8)	5.0 (0.3, NE)	0.9885 (0.4145, 2.3576)	0.9788	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Nervous system disorders; PT: Headache

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]	
HER2 status											
HER2 IHC 1+	214	22 (10.3)	192 (89.7)	NE (NE, NE)	100	6 (6.0)	94 (94.0)	NE (NE, NE)	1.2885 (0.5138, 3.2311) 0.5890	0.5853	0.3413
HER2 IHC 2+/ISH Negative	157	32 (20.4)	125 (79.6)	NE (NE, NE)	72	5 (6.9)	67 (93.1)	NE (11.5, NE)	2.4238 (0.9403, 6.2481) 0.0669	0.0586	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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SOC: Nervous system disorders; PT: Headache

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting									0.4982
1	220	30 (13.6)	190 (86.4) NE (NE, NE)	94	7 (7.4)	87 (92.6) NE (11.5, NE)	1.4240 (0.6208, 3.2663) 0.4040	0.3999	
>=2	150	23 (15.3)	127 (84.7) NE (NE, NE)	78	4 (5.1)	74 (94.9) NE (NE, NE)	2.3357 (0.8001, 6.8188) 0.1207	0.1100	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Nervous system disorders; PT: Headache

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.8768
Yes	233	36 (15.5)	197 (84.5)	NE (NE, NE)	112	8 (7.1)	104 (92.9)	NE (NE, NE)	1.6986 (0.7830, 3.6849) 0.1800	0.1745	
No	98	13 (13.3)	85 (86.7)	NE (NE, NE)	43	3 (7.0)	40 (93.0)	NE (11.5, NE)	1.5927 (0.4518, 5.6151) 0.4691	0.4643	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Nervous system disorders; PT: Headache

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2356
<65	289	49 (17.0)	240 (83.0)	NE (NE, NE)	126	8 (6.3)	118 (93.7)	NE (11.5, NE)	2.0477 (0.9635, 4.3516) 0.0624	0.0571	
>=65	82	5 (6.1)	77 (93.9)	NE (NE, NE)	46	3 (6.5)	43 (93.5)	NE (NE, NE)	0.7609 (0.1786, 3.2406) 0.7116	0.7112	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Nervous system disorders; PT: Headache

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4252
<75	357	53 (14.8)	304 (85.2)	NE (NE, NE)	163	11 (6.7)	152 (93.3)	NE (NE, NE)	1.7047 (0.8846, 3.2852) 0.1110	0.1067	
>=75	14	1 (7.1)	13 (92.9)	NE (5.7, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9985	0.4561	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Headache

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.7177
White	175	31 (17.7)	144 (82.3)	NE (NE, NE)	85	6 (7.1)	79 (92.9)	NE (NE, NE)	2.1204 (0.8801, 5.1082) 0.0939	0.0864	
Non-White	196	23 (11.7)	173 (88.3)	NE (NE, NE)	86	5 (5.8)	81 (94.2)	NE (11.5, NE)	1.4605 (0.5487, 3.8880) 0.4483	0.4446	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Headache

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.4453
Asia	147	15 (10.2)	132 (89.8)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (11.5, NE)	4.1249 (0.5377, 31.6468) 0.1729	0.1397	
North America	58	13 (22.4)	45 (77.6)	NE (10.1, NE)	28	3 (10.7)	25 (89.3)	NE (NE, NE)	1.6464 (0.4643, 5.8388) 0.4401	0.4343	
Europe + Israel	166	26 (15.7)	140 (84.3)	NE (NE, NE)	81	7 (8.6)	74 (91.4)	NE (NE, NE)	1.5728 (0.6798, 3.6388) 0.2900	0.2844	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Headache

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.8217
0	199	36 (18.1)	163 (81.9)	NE (NE, NE)	95	7 (7.4)	88 (92.6)	NE (NE, NE)	1.8506 (0.8178, 4.1875) 0.1396	0.1331	
1	172	18 (10.5)	154 (89.5)	NE (NE, NE)	77	4 (5.2)	73 (94.8)	NE (NE, NE)	1.7218 (0.5775, 5.1338) 0.3296	0.3236	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Headache

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.7052
0	60	10 (16.7)	50 (83.3)	NE (NE, NE)	31	2 (6.5)	29 (93.5)	11.5 (NE, NE)	1.7077 (0.3635, 8.0219) 0.4978	0.4928	
1	107	11 (10.3)	96 (89.7)	NE (NE, NE)	48	4 (8.3)	44 (91.7)	NE (NE, NE)	1.0630 (0.3363, 3.3598) 0.9172	0.9144	
2	114	18 (15.8)	96 (84.2)	NE (NE, NE)	50	2 (4.0)	48 (96.0)	NE (NE, NE)	3.1315 (0.7210, 13.6017) 0.1277	0.1079	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Headache

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 (16.7)	75 (83.3)	NE (NE, NE)	43 (7.0)	40 (93.0)	NE (NE, NE)	1.7929 (0.5120, 6.2780) 0.3612	0.3554	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Nervous system disorders; PT: Headache

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.1428
PD	173	27 (15.6)	146 (84.4)	NE (NE, NE)	77	6 (7.8)	71 (92.2)	NE (NE, NE)	1.6634 (0.6842, 4.0439)	0.2550	
PR	48	10 (20.8)	38 (79.2)	NE (12.4, NE)	21	0	21 (100)	NE (NE, NE)	0.2616 (NE, NE)	0.0744	
SD	82	7 (8.5)	75 (91.5)	NE (NE, NE)	54	3 (5.6)	51 (94.4)	NE (11.5, NE)	0.9811 (0.2474, 3.8905)	0.9784	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.7723
Yes	37	10 (27.0)	27 (73.0)	12.4 (12.4, NE)	13	2 (15.4)	11 (84.6)	NE (2.1, NE)	1.5307 (0.3335, 7.0247) 0.5840	0.5772	
No	334	44 (13.2)	290 (86.8)	NE (NE, NE)	159	9 (5.7)	150 (94.3)	NE (NE, NE)	1.7936 (0.8694, 3.7003) 0.1138	0.1087	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.7676
Yes	24	8 (33.3)	16 (66.7)	12.4 (4.5, NE)	7	1 (14.3)	6 (85.7)	NE (2.1, NE)	2.3444 (0.2915, 18.8558) 0.4231	0.4103	
No	347	46 (13.3)	301 (86.7)	NE (NE, NE)	165	10 (6.1)	155 (93.9)	NE (NE, NE)	1.7064 (0.8554, 3.4040) 0.1293	0.1246	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.6860
Normal Function	201	33 (16.4)	168 (83.6)	NE (NE, NE)	80	7 (8.8)	73 (91.3)	NE (11.5, NE)	1.5616 (0.6864, 3.5529) 0.2879	0.2843	
Mild Impairment	123	19 (15.4)	104 (84.6)	NE (NE, NE)	65	3 (4.6)	62 (95.4)	NE (NE, NE)	2.2221 (0.6446, 7.6604) 0.2060	0.1938	
Moderate Impairment	41	2 (4.9)	39 (95.1)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	0.8944 (0.0804, 9.9443) 0.9277	0.9276	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Nervous system disorders; PT: Headache

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.4844
Normal Function	170	27 (15.9)	143 (84.1)	NE (NE, NE)	88	5 (5.7)	83 (94.3)	NE (NE, NE)	2.3606 (0.9039, 6.1644) 0.0795	0.0706	
Mild Impairment	194	27 (13.9)	167 (86.1)	NE (NE, NE)	82	6 (7.3)	76 (92.7)	NE (NE, NE)	1.3345 (0.5437, 3.2755) 0.5288	0.5270	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Headache

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.6698
Yes	331	48 (14.5)	283 (85.5)	NE (NE, NE)	146	10 (6.8)	136 (93.2)	NE (NE, NE)	1.6770 (0.8435, 3.3343) 0.1403	0.1356	
No	40	6 (15.0)	34 (85.0)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	2.8854 (0.3441, 24.1922) 0.3287	0.3068	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Headache

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.2104
Positive	329	50 (15.2)	279 (84.8)	NE (NE, NE)	152	11 (7.2)	141 (92.8)	NE (NE, NE)	1.6875 (0.8739, 3.2588) 0.1191	0.1147	
Negative	42	4 (9.5)	38 (90.5)	NE (12.4, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) 0.9969	0.3947	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Headache

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.1868
Positive	331	49 (14.8)	282 (85.2)	NE (NE, NE)	155	11 (7.1)	144 (92.9)	NE (NE, NE)	1.6701 (0.8636, 3.2296)	0.1230	
Negative	40	5 (12.5)	35 (87.5)	NE (12.4, NE)	17	0	17 (100)	NE (NE, NE)	0.1275 (NE, NE)	0.3181	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.6561
HER2 IHC 1+	214	8 (3.7)	206 (96.3)	NE (NE, NE)	100	10 (10.0)	90 (90.0)	NE (NE, NE)	0.2993 (0.1171, 0.7652) 0.0118	0.0076	
HER2 IHC 2+/ISH Negative	157	10 (6.4)	147 (93.6)	NE (NE, NE)	72	9 (12.5)	63 (87.5)	NE (NE, NE)	0.3564 (0.1419, 0.8955) 0.0282	0.0222	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.4485
1	220	9 (4.1)	211 (95.9)	NE (NE, NE)	94	11 (11.7)	83 (88.3)	NE (NE, NE)	0.2591 (0.1060, 0.6334) 0.0031	0.0015	
>=2	150	9 (6.0)	141 (94.0)	NE (NE, NE)	78	8 (10.3)	70 (89.7)	NE (NE, NE)	0.4641 (0.1776, 1.2129) 0.1173	0.1086	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.0959
Yes	233	10 (4.3)	223 (95.7)	NE (NE, NE)	112	15 (13.4)	97 (86.6)	NE (NE, NE)	0.1966 (0.0856, 0.4514) 0.0001	<0.0001	
No	98	7 (7.1)	91 (92.9)	NE (NE, NE)	43	3 (7.0)	40 (93.0)	NE (NE, NE)	0.9624 (0.2487, 3.7250) 0.9558	0.9569	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8265
<65	289	14 (4.8)	275 (95.2)	NE (NE, NE)	126	14 (11.1)	112 (88.9)	NE (NE, NE)	0.2994 (0.1397, 0.6415) 0.0019	0.0010	
>=65	82	4 (4.9)	78 (95.1)	NE (NE, NE)	46	5 (10.9)	41 (89.1)	NE (NE, NE)	0.3895 (0.1043, 1.4550) 0.1608	0.1459	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3486
<75	357	18 (5.0)	339 (95.0)	NE (NE, NE)	163	18 (11.0)	145 (89.0)	NE (NE, NE)	0.3307 (0.1697, 0.6445) 0.0012	0.0007	
>=75	14	0	14 (100)	NE (NE, NE)	9	1 (11.1)	8 (88.9)	NE (0.7, NE)	0.0000 (0.0000, ) 0.9984	0.2294	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.3435
White	175	3 (1.7)	172 (98.3)	NE (NE, NE)	85	6 (7.1)	79 (92.9)	NE (NE, NE)	0.1734 (0.0423, 0.7102) 0.0149	0.0063	
Non-White	196	15 (7.7)	181 (92.3)	NE (NE, NE)	86	13 (15.1)	73 (84.9)	NE (NE, NE)	0.3873 (0.1824, 0.8224) 0.0136	0.0105	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.4992
Asia	147	14 (9.5)	133 (90.5)	NE (NE, NE)	63	11 (17.5)	52 (82.5)	NE (NE, NE)	0.4121 (0.1850, 0.9181) 0.0301	0.0251	
North America	58	3 (5.2)	55 (94.8)	NE (14.1, NE)	28	5 (17.9)	23 (82.1)	NE (4.3, NE)	0.1375 (0.0265, 0.7132) 0.0182	0.0058	
Europe + Israel	166	1 (0.6)	165 (99.4)	NE (NE, NE)	81	3 (3.7)	78 (96.3)	NE (NE, NE)	0.1409 (0.0146, 1.3608) 0.0903	0.0484	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.3695
0	199	10 (5.0)	189 (95.0)	NE (NE, NE)	95	13 (13.7)	82 (86.3)	NE (NE, NE)	0.2532 (0.1091, 0.5875) 0.0014	0.0006	
1	172	8 (4.7)	164 (95.3)	NE (NE, NE)	77	6 (7.8)	71 (92.2)	NE (NE, NE)	0.4963 (0.1704, 1.4455) 0.1990	0.1900	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.2043
0	60	1 (1.7)	59 (98.3)	NE (NE, NE)	31	3 (9.7)	28 (90.3)	NE (NE, NE)	0.1517 (0.0157, 1.4653) 0.1031	0.0603	
1	107	3 (2.8)	104 (97.2)	NE (NE, NE)	48	5 (10.4)	43 (89.6)	NE (NE, NE)	0.2253 (0.0535, 0.9477) 0.0420	0.0262	
2	114	11 (9.6)	103 (90.4)	NE (NE, NE)	50	5 (10.0)	45 (90.0)	NE (NE, NE)	0.6808 (0.2297, 2.0177) 0.4880	0.4850	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	3 (3.3)	87 (96.7)	NE (NE, NE)	43	6 (14.0)	37 (86.0)	NE (NE, NE)	0.1862 (0.0457, 0.7591) 0.0191	0.0090	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.5327
PD	173	9 (5.2)	164 (94.8)	NE (NE, NE)	77	5 (6.5)	72 (93.5)	NE (NE, NE)	0.5002 (0.1632, 1.5334)	0.2170	
PR	48	3 (6.3)	45 (93.8)	NE (NE, NE)	21	3 (14.3)	18 (85.7)	NE (NE, NE)	0.2255 (0.0697, 1.7327)	0.1774	
SD	82	5 (6.1)	77 (93.9)	NE (NE, NE)	54	9 (16.7)	45 (83.3)	NE (NE, NE)	0.3476 (0.1028, 0.9338)	0.0279	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.7838
Yes	37	2 (5.4)	35 (94.6)	NE (NE, NE)	13	2 (15.4)	11 (84.6)	NE (2.3, NE)	0.2224 (0.0289, 1.7119)	0.1170	
No	334	16 (4.8)	318 (95.2)	NE (NE, NE)	159	17 (10.7)	142 (89.3)	NE (NE, NE)	0.3341 (0.1666, 0.6698)	0.0012	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.8723
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	1 (14.3)	6 (85.7)	NE (2.3, NE)	0.3100 (0.0194, 4.9570) 0.4076	0.3809	
No	347	17 (4.9)	330 (95.1)	NE (NE, NE)	165	18 (10.9)	147 (89.1)	NE (NE, NE)	0.3278 (0.1667, 0.6443) 0.0012	0.0007	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.4266
Normal Function	201	6 (3.0)	195 (97.0)	NE (NE, NE)	80	7 (8.8)	73 (91.3)	NE (NE, NE)	0.2011 (0.0624, 0.6476) 0.0072	0.0030	
Mild Impairment	123	11 (8.9)	112 (91.1)	NE (NE, NE)	65	8 (12.3)	57 (87.7)	NE (NE, NE)	0.5471 (0.2165, 1.3825) 0.2022	0.1960	
Moderate Impairment	41	1 (2.4)	40 (97.6)	NE (NE, NE)	23	3 (13.0)	20 (87.0)	NE (NE, NE)	0.1694 (0.0176, 1.6307) 0.1244	0.0809	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.0631
Normal Function	170	7 (4.1)	163 (95.9)	NE (NE, NE)	88	14 (15.9)	74 (84.1)	NE (NE, NE)	0.2069 (0.0830, 0.5158) 0.0007	0.0002	
Mild Impairment	194	11 (5.7)	183 (94.3)	NE (NE, NE)	82	5 (6.1)	77 (93.9)	NE (NE, NE)	0.6452 (0.2189, 1.9019) 0.4269	0.4242	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.2920
Yes	331	16 (4.8)	315 (95.2)	NE (NE, NE)	146	14 (9.6)	132 (90.4)	NE (NE, NE)	0.3749 (0.1809, 0.7770) 0.0083	0.0061	
No	40	2 (5.0)	38 (95.0)	NE (NE, NE)	26	5 (19.2)	21 (80.8)	NE (NE, NE)	0.2066 (0.0394, 1.0839) 0.0622	0.0403	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.9266
Positive	329	17 (5.2)	312 (94.8)	NE (NE, NE)	152	18 (11.8)	134 (88.2)	NE (NE, NE)	0.3224 (0.1643, 0.6327)	0.0005	
Negative	42	1 (2.4)	41 (97.6)	NE (NE, NE)	20	1 (5.0)	19 (95.0)	NE (NE, NE)	0.3986 (0.0247, 6.4426)	0.5024	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.9708
Positive	331	17 (5.1)	314 (94.9)	NE (NE, NE)	155	18 (11.6)	137 (88.4)	NE (NE, NE)	0.3245 (0.1654, 0.6367)	0.0006	
Negative	40	1 (2.5)	39 (97.5)	NE (NE, NE)	17	1 (5.9)	16 (94.1)	NE (NE, NE)	0.4177 (0.0261, 6.6782)	0.5239	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.5377
HER2 IHC 1+	214	76 (35.5)	138 (64.5)	19.6 (12.1, NE)	100	29 (29.0)	71 (71.0)	11.8 (6.8, NE)	0.8068 (0.5198, 1.2523) 0.3386	0.3395	
HER2 IHC 2+/ISH Negative	157	60 (38.2)	97 (61.8)	16.5 (9.0, NE)	72	27 (37.5)	45 (62.5)	6.9 (4.0, NE)	0.6434 (0.4020, 1.0297) 0.0660	0.0634	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.1836
1	220	82 (37.3)	138 (62.7)	19.6 (9.0, NE)	94	37 (39.4)	57 (60.6)	6.1 (3.7, NE)	0.6157 (0.4134, 0.9170) 0.0170	0.0160	
>=2	150	53 (35.3)	97 (64.7)	16.5 (11.7, NE)	78	19 (24.4)	59 (75.6)	11.8 (6.8, NE)	0.9239 (0.5367, 1.5903) 0.7752	0.7734	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.9272
Yes	233	89 (38.2)	144 (61.8)	12.9 (9.0, NE)	112	38 (33.9)	74 (66.1)	11.0 (6.0, NE)	0.7167 (0.4838, 1.0618) 0.0967	0.0946	
No	98	40 (40.8)	58 (59.2)	22.7 (9.0, NE)	43	17 (39.5)	26 (60.5)	6.8 (3.8, NE)	0.7022 (0.3935, 1.2529) 0.2314	0.2293	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8942
<65	289	109 (37.7)	180 (62.3)	13.5 (11.7, NE)	126	41 (32.5)	85 (67.5)	11.0 (6.1, NE)	0.7198 (0.4963, 1.0440) 0.0831	0.0818	
>=65	82	27 (32.9)	55 (67.1)	NE (7.8, NE)	46	15 (32.6)	31 (67.4)	NE (4.0, NE)	0.7737 (0.4088, 1.4644) 0.4306	0.4276	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3081
<75	357	131 (36.7)	226 (63.3)	16.5 (12.1, NE)	163	54 (33.1)	109 (66.9)	11.0 (6.1, NE)	0.6990 (0.5037, 0.9700) 0.0322	0.0314	
>=75	14	5 (35.7)	9 (64.3)	NE (2.1, NE)	9	2 (22.2)	7 (77.8)	NE (3.7, NE)	1.4453 (0.2753, 7.5889) 0.6633	0.6616	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.8106
White	175	76 (43.4)	99 (56.6)	12.1 (7.0, NE)	85	31 (36.5)	54 (63.5)	6.9 (3.8, 11.0)	0.7579 (0.4917, 1.1681) 0.2092	0.2076	
Non-White	196	60 (30.6)	136 (69.4)	19.6 (12.5, NE)	86	25 (29.1)	61 (70.9)	11.8 (6.8, NE)	0.6939 (0.4299, 1.1199) 0.1345	0.1328	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.7152
Asia	147	39 (26.5)	108 (73.5)	NE (19.6, NE)	63	12 (19.0)	51 (81.0)	NE (NE, NE)	0.9932 (0.5139, 1.9194) 0.9837	0.9831	
North America	58	27 (46.6)	31 (53.4)	9.0 (4.9, 16.5)	28	12 (42.9)	16 (57.1)	6.0 (2.1, NE)	0.6294 (0.3059, 1.2949) 0.2084	0.2064	
Europe + Israel	166	70 (42.2)	96 (57.8)	10.8 (7.6, NE)	81	32 (39.5)	49 (60.5)	6.9 (3.8, 11.8)	0.6551 (0.4247, 1.0104) 0.0557	0.0542	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.7795
0	199	75 (37.7)	124 (62.3)	16.5 (10.5, NE)	95	29 (30.5)	66 (69.5)	11.0 (6.8, NE)	0.7677 (0.4946, 1.1915) 0.2385	0.2390	
1	172	61 (35.5)	111 (64.5)	12.6 (10.0, NE)	77	27 (35.1)	50 (64.9)	6.9 (4.0, 11.8)	0.6791 (0.4240, 1.0875) 0.1072	0.1044	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1605
0	60	15 (25.0)	45 (75.0)	NE (10.8, NE)	31	5 (16.1)	26 (83.9)	NE (NE, NE)	1.1377 (0.4051, 3.1951) 0.8066	0.8070	
1	107	35 (32.7)	72 (67.3)	19.6 (9.0, NE)	48	22 (45.8)	26 (54.2)	6.9 (2.3, NE)	0.4845 (0.2808, 0.8361) 0.0092	0.0079	
2	114	49 (43.0)	65 (57.0)	12.5 (7.8, NE)	50	20 (40.0)	30 (60.0)	6.8 (2.7, 11.8)	0.6531 (0.3798, 1.1229) 0.1234	0.1199	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	37 (41.1)	53 (58.9)	12.1 (7.1, NE)	43	9 (20.9)	34 (79.1)	NE (3.7, NE)	1.2260 (0.5801, 2.5911) 0.5936	0.5922	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.3386
PD	173	62 (35.8)	111 (64.2)	22.7 (9.0, NE)	77	21 (27.3)	56 (72.7)	11.8 (6.0, 11.8)	0.8530 (0.5137, 1.4165)	0.5379	
PR	48	17 (35.4)	31 (64.6)	19.6 (10.0, 19.6)	21	6 (28.6)	15 (71.4)	NE (6.8, NE)	0.5390 (0.3289, 2.2162)	0.7529	
SD	82	23 (28.0)	59 (72.0)	NE (12.9, NE)	54	19 (35.2)	35 (64.8)	6.9 (3.7, NE)	0.5140 (0.2734, 0.9662)	0.0359	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.4176
Yes	37	15 (40.5)	22 (59.5)	12.1 (3.7, NE)	13	3 (23.1)	10 (76.9)	6.9 (1.4, NE)	1.2030 (0.3385, 4.2755) 0.7751	0.7743	
No	334	121 (36.2)	213 (63.8)	19.6 (12.4, NE)	159	53 (33.3)	106 (66.7)	11.0 (6.1, NE)	0.7028 (0.5039, 0.9801) 0.0376	0.0369	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.9084
Yes	24	7 (29.2)	17 (70.8)	NE (3.0, NE)	7	2 (28.6)	5 (71.4)	6.9 (0.3, NE)	0.9041 (0.1857, 4.4019) 0.9006	0.8951	
No	347	129 (37.2)	218 (62.8)	16.5 (11.7, NE)	165	54 (32.7)	111 (67.3)	11.0 (6.1, NE)	0.7220 (0.5203, 1.0019) 0.0514	0.0506	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.3407
Normal Function	201	71 (35.3)	130 (64.7)	19.6 (12.5, NE)	80	27 (33.8)	53 (66.3)	NE (6.0, NE)	0.6975 (0.4427, 1.0992) 0.1206	0.1207	
Mild Impairment	123	45 (36.6)	78 (63.4)	12.4 (9.0, NE)	65	21 (32.3)	44 (67.7)	11.0 (6.8, 11.8)	0.6332 (0.3681, 1.0892) 0.0987	0.0954	
Moderate Impairment	41	19 (46.3)	22 (53.7)	8.0 (4.9, NE)	23	7 (30.4)	16 (69.6)	6.9 (3.7, NE)	1.2876 (0.5348, 3.1000) 0.5728	0.5734	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1836
Normal Function	170	69 (40.6)	101 (59.4)	13.5 (10.0, NE)	88	27 (30.7)	61 (69.3)	NE (6.0, NE)	0.8703 (0.5513, 1.3738) 0.5508	0.5491	
Mild Impairment	194	65 (33.5)	129 (66.5)	NE (10.5, NE)	82	29 (35.4)	53 (64.6)	11.0 (3.7, 11.8)	0.5913 (0.3755, 0.9309) 0.0233	0.0218	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.0423
Yes	331	118 (35.6)	213 (64.4)	19.6 (12.1, NE)	146	52 (35.6)	94 (64.4)	11.0 (6.0, NE)	0.6412 (0.4580, 0.8978) 0.0097	0.0092	
No	40	18 (45.0)	22 (55.0)	12.4 (4.9, NE)	26	4 (15.4)	22 (84.6)	NE (NE, NE)	2.0751 (0.6869, 6.2690) 0.1956	0.1863	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.6198
Positive	329	127 (38.6)	202 (61.4)	13.5 (11.7, NE)	152	53 (34.9)	99 (65.1)	11.0 (6.0, NE)	0.7127 (0.5124, 0.9911)	0.0433	
Negative	42	9 (21.4)	33 (78.6)	NE (10.8, NE)	20	3 (15.0)	17 (85.0)	NE (NE, NE)	1.0086 (0.2576, 3.9494)	0.9902	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.4001
Positive	331	130 (39.3)	201 (60.7)	13.5 (10.5, NE)	155	55 (35.5)	100 (64.5)	11.0 (6.0, NE)	0.7240 (0.5235, 1.0013)	0.0499	
Negative	40	6 (15.0)	34 (85.0)	NE (10.8, NE)	17	1 (5.9)	16 (94.1)	NE (NE, NE)	1.3221 (0.1439, 12.1501)	0.8045	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.9434
HER2 IHC 1+	214	26 (12.1)	188 (87.9)	NE (22.7, NE)	100	12 (12.0)	88 (88.0)	NE (9.6, NE)	0.5438 (0.2656, 1.1133) 0.0957	0.0910	
HER2 IHC 2+/ISH Negative	157	17 (10.8)	140 (89.2)	NE (NE, NE)	72	8 (11.1)	64 (88.9)	NE (11.5, NE)	0.5184 (0.2152, 1.2488) 0.1430	0.1369	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.3371
1	220	26 (11.8)	194 (88.2)	NE (22.7, NE)	94	14 (14.9)	80 (85.1)	NE (11.5, NE)	0.4762 (0.2424, 0.9355) 0.0313	0.0278	
>=2	150	16 (10.7)	134 (89.3)	NE (NE, NE)	78	6 (7.7)	72 (92.3)	NE (9.6, NE)	0.6450 (0.2403, 1.7308) 0.3839	0.3803	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.5246
Yes	233	26 (11.2)	207 (88.8)	NE (NE, NE)	112	14 (12.5)	98 (87.5)	NE (11.5, NE)	0.4995 (0.2529, 0.9867) 0.0457	0.0418	
No	98	15 (15.3)	83 (84.7)	NE (22.7, NE)	43	6 (14.0)	37 (86.0)	NE (9.6, NE)	0.6228 (0.2342, 1.6561) 0.3426	0.3385	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2319
<65	289	38 (13.1)	251 (86.9)	NE (22.7, NE)	126	14 (11.1)	112 (88.9)	NE (11.5, NE)	0.6265 (0.3305, 1.1876) 0.1518	0.1487	
>=65	82	5 (6.1)	77 (93.9)	NE (NE, NE)	46	6 (13.0)	40 (87.0)	NE (9.6, NE)	0.2826 (0.0823, 0.9701) 0.0446	0.0333	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9421
<75	357	42 (11.8)	315 (88.2)	NE (22.7, NE)	163	19 (11.7)	144 (88.3)	NE (11.5, NE)	0.5209 (0.2941, 0.9226) 0.0253	0.0231	
>=75	14	1 (7.1)	13 (92.9)	NE (NE, NE)	9	1 (11.1)	8 (88.9)	NE (5.5, NE)	0.5025 (0.0313, 8.0623) 0.6270	0.6202	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.5133
White	175	25 (14.3)	150 (85.7)	22.7 (22.7, NE)	85	13 (15.3)	72 (84.7)	11.6 (11.5, NE)	0.3730 (0.1800, 0.7729) 0.0080	0.0060	
Non-White	196	18 (9.2)	178 (90.8)	NE (NE, NE)	86	7 (8.1)	79 (91.9)	NE (9.6, NE)	0.7716 (0.3158, 1.8854) 0.5696	0.5685	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.0540
Asia	147	12 (8.2)	135 (91.8)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (NE, NE)	3.8409 (0.4942, 29.8507) 0.1983	0.1665	
North America	58	10 (17.2)	48 (82.8)	NE (12.9, NE)	28	7 (25.0)	21 (75.0)	NE (2.7, NE)	0.2762 (0.0926, 0.8240) 0.0211	0.0143	
Europe + Israel	166	21 (12.7)	145 (87.3)	22.7 (22.7, NE)	81	12 (14.8)	69 (85.2)	11.6 (9.6, NE)	0.3698 (0.1727, 0.7917) 0.0104	0.0080	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.0027
0	199	22 (11.1)	177 (88.9)	NE (NE, NE)	95	17 (17.9)	78 (82.1)	11.6 (9.6, NE)	0.2977 (0.1521, 0.5825) 0.0004	0.0002	
1	172	21 (12.2)	151 (87.8)	22.7 (22.7, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	1.8758 (0.5455, 6.4499) 0.3182	0.3108	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.0610
0	60	5 (8.3)	55 (91.7)	NE (NE, NE)	31	1 (3.2)	30 (96.8)	NE (NE, NE)	1.4382 (0.1547, 13.3688) 0.7494	0.7480	
1	107	13 (12.1)	94 (87.9)	NE (NE, NE)	48	10 (20.8)	38 (79.2)	11.6 (11.5, NE)	0.3422 (0.1464, 0.7999) 0.0133	0.0098	
2	114	13 (11.4)	101 (88.6)	NE (22.7, NE)	50	8 (16.0)	42 (84.0)	9.6 (9.6, NE)	0.3980 (0.1542, 1.0275) 0.0569	0.0493	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	12 (13.3)	78 (86.7)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	2.7133 (0.3437, 21.4202) 0.3437	0.3248	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.7555
PD	173	22 (12.7)	151 (87.3)	NE (22.7, NE)	77	8 (10.4)	69 (89.6)	NE (NE, NE)	0.6652 (0.2868, 1.5429)	0.3402	
PR	48	4 (8.3)	44 (91.7)	NE (NE, NE)	21	2 (9.5)	19 (90.5)	9.6 (9.6, NE)	0.5292 (0.0879, 3.1847)	0.4805	
SD	82	8 (9.8)	74 (90.2)	NE (NE, NE)	54	7 (13.0)	47 (87.0)	NE (11.5, NE)	0.4421 (0.1530, 1.2776)	0.1230	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.0354
Yes	37	6 (16.2)	31 (83.8)	NE (16.2, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9956	0.2224	
No	334	37 (11.1)	297 (88.9)	NE (22.7, NE)	159	20 (12.6)	139 (87.4)	NE (11.5, NE)	0.4645 (0.2618, 0.8240) 0.0087	0.0074	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0448
Yes	24	5 (20.8)	19 (79.2)	NE (8.4, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9960	0.2697	
No	347	38 (11.0)	309 (89.0)	NE (22.7, NE)	165	20 (12.1)	145 (87.9)	NE (11.5, NE)	0.4597 (0.2593, 0.8149) 0.0078	0.0065	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.5245
Normal Function	201	22 (10.9)	179 (89.1)	NE (NE, NE)	80	6 (7.5)	74 (92.5)	NE (NE, NE)	0.8644 (0.3390, 2.2042) 0.7602	0.7611	
Mild Impairment	123	17 (13.8)	106 (86.2)	NE (22.7, NE)	65	9 (13.8)	56 (86.2)	11.5 (9.6, NE)	0.4769 (0.2016, 1.1284) 0.0920	0.0857	
Moderate Impairment	41	4 (9.8)	37 (90.2)	NE (NE, NE)	23	5 (21.7)	18 (78.3)	NE (5.5, NE)	0.2792 (0.0738, 1.0562) 0.0602	0.0454	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.7179
Normal Function	170	22 (12.9)	148 (87.1)	NE (22.7, NE)	88	12 (13.6)	76 (86.4)	NE (9.6, NE)	0.4945 (0.2357, 1.0375) 0.0625	0.0580	
Mild Impairment	194	21 (10.8)	173 (89.2)	NE (NE, NE)	82	8 (9.8)	74 (90.2)	NE (11.5, NE)	0.6003 (0.2567, 1.4039) 0.2390	0.2335	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.8322
Yes	331	36 (10.9)	295 (89.1)	NE (22.7, NE)	146	17 (11.6)	129 (88.4)	NE (11.5, NE)	0.5068 (0.2775, 0.9255) 0.0270	0.0244	
No	40	7 (17.5)	33 (82.5)	NE (NE, NE)	26	3 (11.5)	23 (88.5)	NE (NE, NE)	0.8060 (0.1900, 3.4200) 0.7699	0.7696	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.9339
Positive	329	41 (12.5)	288 (87.5)	NE (22.7, NE)	152	19 (12.5)	133 (87.5)	NE (11.5, NE)	0.5428 (0.3077, 0.9576)	0.0324	
Negative	42	2 (4.8)	40 (95.2)	NE (10.8, NE)	20	1 (5.0)	19 (95.0)	NE (NE, NE)	0.4161 (0.0258, 6.7118)	0.5236	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.2403
Positive	331	41 (12.4)	290 (87.6)	NE (22.7, NE)	155	20 (12.9)	135 (87.1)	NE (11.5, NE)	0.5238 (0.2996, 0.9159)	0.0212	
Negative	40	2 (5.0)	38 (95.0)	NE (10.8, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) 0.9981	0.5839	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.6087
HER2 IHC 1+	214	70 (32.7)	144 (67.3)	21.3 (12.7, NE)	100	18 (18.0)	82 (82.0)	NE (NE, NE)	1.2648 (0.7463, 2.1434) 0.3828	0.3827	
HER2 IHC 2+/ISH Negative	157	57 (36.3)	100 (63.7)	12.7 (8.9, NE)	72	18 (25.0)	54 (75.0)	NE (NE, NE)	1.0006 (0.5844, 1.7130) 0.9984	0.9969	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.0619
1	220	72 (32.7)	148 (67.3)	18.0 (12.3, NE)	94	14 (14.9)	80 (85.1)	NE (NE, NE)	1.6332 (0.9158, 2.9126) 0.0965	0.0936	
>=2	150	55 (36.7)	95 (63.3)	12.8 (9.7, NE)	78	22 (28.2)	56 (71.8)	NE (6.3, NE)	0.8147 (0.4895, 1.3558) 0.4303	0.4283	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											
Yes	233	77 (33.0)	156 (67.0)	18.0 (12.2, NE)	112	16 (14.3)	96 (85.7)	NE (7.1, NE)	1.5173 (0.8744, 2.6328) 0.1382	0.1355	0.1158
No	98	29 (29.6)	69 (70.4)	NE (12.8, NE)	43	12 (27.9)	31 (72.1)	NE (NE, NE)	0.7726 (0.3931, 1.5188) 0.4544	0.4539	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5366
<65	289	96 (33.2)	193 (66.8)	18.6 (12.4, NE)	126	26 (20.6)	100 (79.4)	NE (NE, NE)	1.0740 (0.6907, 1.6700) 0.7514	0.7527	
>=65	82	31 (37.8)	51 (62.2)	12.7 (8.1, NE)	46	10 (21.7)	36 (78.3)	NE (6.3, NE)	1.3532 (0.6583, 2.7813) 0.4107	0.4078	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7807
<75	357	121 (33.9)	236 (66.1)	18.0 (12.4, NE)	163	33 (20.2)	130 (79.8)	NE (NE, NE)	1.1222 (0.7577, 1.6619) 0.5651	0.5666	
>=75	14	6 (42.9)	8 (57.1)	6.5 (3.0, NE)	9	3 (33.3)	6 (66.7)	NE (0.6, NE)	1.2545 (0.3124, 5.0381) 0.7493	0.7488	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.6617
White	175	58 (33.1)	117 (66.9)	18.6 (12.2, NE)	85	17 (20.0)	68 (80.0)	NE (7.1, NE)	1.0126 (0.5811, 1.7645) 0.9647	0.9649	
Non-White	196	69 (35.2)	127 (64.8)	14.9 (11.7, NE)	86	18 (20.9)	68 (79.1)	NE (NE, NE)	1.2943 (0.7666, 2.1853) 0.3343	0.3328	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.9280
Asia	147	49 (33.3)	98 (66.7)	NE (11.9, NE)	63	13 (20.6)	50 (79.4)	NE (NE, NE)	1.2051 (0.6500, 2.2341) 0.5536	0.5519	
North America	58	24 (41.4)	34 (58.6)	18.0 (5.5, NE)	28	6 (21.4)	22 (78.6)	NE (3.1, NE)	1.3091 (0.5240, 3.2709) 0.5642	0.5669	
Europe + Israel	166	54 (32.5)	112 (67.5)	18.6 (12.2, NE)	81	17 (21.0)	64 (79.0)	NE (NE, NE)	1.0165 (0.5824, 1.7739) 0.9542	0.9566	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.7299
0	199	68 (34.2)	131 (65.8)	18.0 (12.2, NE)	95	20 (21.1)	75 (78.9)	NE (NE, NE)	1.0644 (0.6409, 1.7676) 0.8096	0.8102	
1	172	59 (34.3)	113 (65.7)	21.3 (11.5, NE)	77	16 (20.8)	61 (79.2)	NE (NE, NE)	1.2240 (0.6980, 2.1465) 0.4806	0.4817	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.3907
0	60	28 (46.7)	32 (53.3)	8.0 (4.3, NE)	31	13 (41.9)	18 (58.1)	4.4 (2.3, NE)	0.7734 (0.3973, 1.5056) 0.4496	0.4474	
1	107	33 (30.8)	74 (69.2)	NE (12.7, NE)	48	9 (18.8)	39 (81.3)	NE (NE, NE)	1.3543 (0.6450, 2.8439) 0.4230	0.4214	
2	114	38 (33.3)	76 (66.7)	12.8 (11.5, NE)	50	10 (20.0)	40 (80.0)	NE (7.1, NE)	0.9475 (0.4606, 1.9493) 0.8836	0.8838	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]		
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	28 (31.1)	62 (68.9)	43	4 (9.3)	39 (90.7)	18.6 (14.9, NE)	NE (NE, NE)	2.1025 (0.7228, 6.1157) 0.1726	0.1631

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.9388
PD	173	53 (30.6)	120 (69.4)	18.6 (12.7, NE)	77	17 (22.1)	60 (77.9)	NE (7.1, NE)	0.9293 (0.5307, 1.6274) 0.7976	0.7965	
PR	48	14 (29.2)	34 (70.8)	NE (11.7, NE)	21	3 (14.3)	18 (85.7)	NE (NE, NE)	1.5133 (0.4298, 5.3279) 0.5189	0.5170	
SD	82	32 (39.0)	50 (61.0)	12.8 (9.7, NE)	54	14 (25.9)	40 (74.1)	NE (4.4, NE)	1.0423 (0.5500, 1.9752) 0.8989	0.8982	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.5325
Yes	37	12 (32.4)	25 (67.6)	18.6 (5.0, NE)	13	3 (23.1)	10 (76.9)	NE (0.7, NE)	0.8291 (0.2253, 3.0506)	0.7819	
No	334	115 (34.4)	219 (65.6)	18.0 (12.3, NE)	159	33 (20.8)	126 (79.2)	NE (NE, NE)	1.1625 (0.7846, 1.7224)	0.4540	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.4643
Yes	24	7 (29.2)	17 (70.8)	18.6 (8.0, NE)	7	2 (28.6)	5 (71.4)	NE (0.1, NE)	0.5061 (0.0962, 2.6613) 0.4213	0.4126	
No	347	120 (34.6)	227 (65.4)	18.0 (12.3, NE)	165	34 (20.6)	131 (79.4)	NE (NE, NE)	1.1814 (0.8026, 1.7390) 0.3981	0.3989	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.5237
Normal Function	201	66 (32.8)	135 (67.2)	18.6 (12.4, NE)	80	12 (15.0)	68 (85.0)	NE (NE, NE)	1.5202 (0.8151, 2.8351) 0.1878	0.1850	
Mild Impairment	123	42 (34.1)	81 (65.9)	NE (9.7, NE)	65	14 (21.5)	51 (78.5)	NE (7.1, NE)	1.0366 (0.5576, 1.9270) 0.9095	0.9085	
Moderate Impairment	41	15 (36.6)	26 (63.4)	12.3 (11.5, NE)	23	8 (34.8)	15 (65.2)	NE (3.1, NE)	0.9358 (0.3955, 2.2145) 0.8801	0.8800	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.9087
Normal Function	170	66 (38.8)	104 (61.2)	12.8 (11.5, NE)	88	21 (23.9)	67 (76.1)	NE (NE, NE)	1.1557 (0.7031, 1.8997) 0.5681	0.5680	
Mild Impairment	194	56 (28.9)	138 (71.1)	18.6 (12.7, NE)	82	13 (15.9)	69 (84.1)	NE (NE, NE)	1.1862 (0.6394, 2.2006) 0.5881	0.5880	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1689
Yes	331	114 (34.4)	217 (65.6)	18.0 (12.3, NE)	146	28 (19.2)	118 (80.8)	NE (NE, NE)	1.2602 (0.8284, 1.9170) 0.2799	0.2790	
No	40	13 (32.5)	27 (67.5)	NE (5.8, NE)	26	8 (30.8)	18 (69.2)	NE (2.9, NE)	0.6220 (0.2484, 1.5573) 0.3106	0.3068	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.1796
Positive	329	106 (32.2)	223 (67.8)	18.6 (12.7, NE)	152	26 (17.1)	126 (82.9)	NE (NE, NE)	1.2663 (0.8191, 1.9576) 0.2882	0.2872	
Negative	42	21 (50.0)	21 (50.0)	6.5 (3.0, NE)	20	10 (50.0)	10 (50.0)	2.9 (1.2, NE)	0.7709 (0.3548, 1.6749) 0.5110	0.5058	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (derived)											0.2759
Positive	331	107 (32.3)	224 (67.7)	18.6 (12.7, NE)	155	28 (18.1)	127 (81.9)	NE (NE, NE)	1.2059 (0.7900, 1.8407) 0.3856	0.3853	
Negative	40	20 (50.0)	20 (50.0)	6.5 (2.3, NE)	17	8 (47.1)	9 (52.9)	3.7 (1.0, NE)	0.7860 (0.3371, 1.8327) 0.5772	0.5735	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0020
HER2 IHC 1+	214	28 (13.1)	186 (86.9)	NE (NE, NE)	100	17 (17.0)	83 (83.0)	NE (11.3, NE)	0.4233 (0.2257, 0.7939) 0.0074	0.0059	
HER2 IHC 2+/ISH Negative	157	32 (20.4)	125 (79.6)	NE (NE, NE)	72	4 (5.6)	68 (94.4)	NE (9.9, NE)	2.8684 (1.0064, 8.1756) 0.0486	0.0393	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.1907
1	220	33 (15.0)	187 (85.0)	NE (NE, NE)	94	14 (14.9)	80 (85.1)	NE (9.9, NE)	0.5918 (0.3104, 1.1284) 0.1111	0.1071
>=2	150	27 (18.0)	123 (82.0)	NE (NE, NE)	78	7 (9.0)	71 (91.0)	NE (NE, NE)	1.5252 (0.6569, 3.5415) 0.3260	0.3224

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.8881
Yes	233	42 (18.0)	191 (82.0)	NE (NE, NE)	112	16 (14.3)	96 (85.7)	NE (9.9, NE)	0.7609 (0.4184, 1.3838) 0.3705	0.3678	
No	98	11 (11.2)	87 (88.8)	NE (NE, NE)	43	4 (9.3)	39 (90.7)	NE (11.3, NE)	0.8783 (0.2758, 2.7968) 0.8262	0.8261	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2683
<65	289	39 (13.5)	250 (86.5)	NE (NE, NE)	126	14 (11.1)	112 (88.9)	NE (9.9, NE)	0.7465 (0.3977, 1.4012) 0.3628	0.3608	
>=65	82	21 (25.6)	61 (74.4)	NE (NE, NE)	46	7 (15.2)	39 (84.8)	NE (11.3, NE)	1.3559 (0.5722, 3.2132) 0.4891	0.4870	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3362
<75	357	55 (15.4)	302 (84.6)	NE (NE, NE)	163	19 (11.7)	144 (88.3)	NE (9.9, NE)	0.8576 (0.5015, 1.4668) 0.5749	0.5737	
>=75	14	5 (35.7)	9 (64.3)	6.2 (3.9, NE)	9	2 (22.2)	7 (77.8)	NE (2.1, NE)	1.9361 (0.3680, 10.1858) 0.4355	0.4277	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.4975
White	175	38 (21.7)	137 (78.3)	NE (NE, NE)	85	12 (14.1)	73 (85.9)	NE (NE, NE)	1.0062 (0.5170, 1.9584) 0.9855	0.9871	
Non-White	196	22 (11.2)	174 (88.8)	NE (NE, NE)	86	9 (10.5)	77 (89.5)	NE (9.9, NE)	0.6770 (0.3050, 1.5025) 0.3376	0.3358	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.0212
Asia	147	17 (11.6)	130 (88.4)	NE (NE, NE)	63	3 (4.8)	60 (95.2)	NE (9.9, NE)	1.4080 (0.4028, 4.9225) 0.5920	0.5900	
North America	58	10 (17.2)	48 (82.8)	NE (NE, NE)	28	9 (32.1)	19 (67.9)	NE (2.1, NE)	0.3456 (0.1366, 0.8743) 0.0248	0.0192	
Europe + Israel	166	33 (19.9)	133 (80.1)	NE (NE, NE)	81	9 (11.1)	72 (88.9)	NE (NE, NE)	1.2122 (0.5712, 2.5725) 0.6163	0.6164	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
ECOG PS											
0	199	34 (17.1)	165 (82.9)	NE (NE, NE)	95	12 (12.6)	83 (87.4)	NE (9.9, NE)	0.8966 (0.4582, 1.7544) 0.7500	0.7482	0.9236
1	172	26 (15.1)	146 (84.9)	NE (NE, NE)	77	9 (11.7)	68 (88.3)	NE (11.3, NE)	0.8102 (0.3695, 1.7766) 0.5994	0.5985	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(1/2)										0.8006
0	60	7 (11.7)	53 (88.3)	NE (NE, NE)	31	4 (12.9)	27 (87.1)	NE (3.9, NE)	0.5438 (0.1550, 1.9082) 0.3415	0.3345
1	107	16 (15.0)	91 (85.0)	NE (NE, NE)	48	7 (14.6)	41 (85.4)	NE (11.3, NE)	0.7109 (0.2892, 1.7471) 0.4570	0.4551
2	114	19 (16.7)	95 (83.3)	NE (NE, NE)	50	6 (12.0)	44 (88.0)	NE (NE, NE)	0.9339 (0.3644, 2.3938) 0.8868	0.8864

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	18 (20.0)	72 (80.0)	NE (NE, NE)	43	4 (9.3)	39 (90.7)	NE (9.9, NE)	1.4815 (0.4875, 4.5022) 0.4883	0.4877	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.4762
PD	173	28 (16.2)	145 (83.8)	NE (NE, NE)	77	8 (10.4)	69 (89.6)	NE (NE, NE)	1.0765 (0.4813, 2.4082)	0.8575	0.8576
PR	48	11 (22.9)	37 (77.1)	NE (14.0, NE)	21	2 (9.5)	19 (90.5)	NE (4.8, NE)	1.5683 (0.3401, 7.2317)	0.5639	0.5607
SD	82	12 (14.6)	70 (85.4)	NE (NE, NE)	54	9 (16.7)	45 (83.3)	NE (9.9, NE)	0.4990 (0.2043, 1.2188)	0.1271	0.1208

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Reported history of CNS metastases											0.1159
Yes	37	5 (13.5)	32 (86.5)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9961	0.2778	
No	334	55 (16.5)	279 (83.5)	NE (NE, NE)	159	21 (13.2)	138 (86.8)	NE (11.3, NE)	0.8124 (0.4849, 1.3611) 0.4301	0.4292	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.9216
Yes	24	4 (16.7)	20 (83.3)	NE (11.1, NE)	7	1 (14.3)	6 (85.7)	NE (3.9, NE)	0.8785 (0.0961, 8.0271) 0.9086	0.9086	
No	347	56 (16.1)	291 (83.9)	NE (NE, NE)	165	20 (12.1)	145 (87.9)	NE (11.3, NE)	0.8672 (0.5138, 1.4636) 0.5935	0.5926	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.7133
Normal Function	201	26 (12.9)	175 (87.1)	NE (NE, NE)	80	8 (10.0)	72 (90.0)	NE (9.9, NE)	0.7624 (0.3349, 1.7354) 0.5179	0.5169	
Mild Impairment	123	25 (20.3)	98 (79.7)	NE (NE, NE)	65	7 (10.8)	58 (89.2)	NE (NE, NE)	1.1304 (0.4764, 2.6824) 0.7810	0.7815	
Moderate Impairment	41	9 (22.0)	32 (78.0)	NE (NE, NE)	23	6 (26.1)	17 (73.9)	NE (3.7, NE)	0.7534 (0.2675, 2.1224) 0.5921	0.5922	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.5151
Normal Function	170	26 (15.3)	144 (84.7)	NE (NE, NE)	88	12 (13.6)	76 (86.4)	NE (NE, NE)	0.7568 (0.3765, 1.5215) 0.4342	0.4323	
Mild Impairment	194	34 (17.5)	160 (82.5)	NE (NE, NE)	82	9 (11.0)	73 (89.0)	11.3 (11.3, NE)	0.9884 (0.4639, 2.1062) 0.9760	0.9755	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline visceral disease										0.1425
Yes	331	56 (16.9)	275 (83.1)	NE (NE, NE)	146	17 (11.6)	129 (88.4)	NE (11.3, NE)	0.9844 (0.5658, 1.7124)	0.9546
No	40	4 (10.0)	36 (90.0)	NE (NE, NE)	26	4 (15.4)	22 (84.6)	NE (3.1, NE)	0.3499 (0.0822, 1.4897)	0.1402

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (IXRS)										0.9614
Positive	329	52 (15.8)	277 (84.2)	NE (NE, NE)	152	18 (11.8)	134 (88.2)	NE (11.3, NE)	0.8730 (0.5045, 1.5109)	0.6261
Negative	42	8 (19.0)	34 (81.0)	NE (9.7, NE)	20	3 (15.0)	17 (85.0)	NE (3.1, NE)	0.7977 (0.2008, 3.1686)	0.7476

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (derived)											0.4919
Positive	331	54 (16.3)	277 (83.7)	NE (NE, NE)	155	20 (12.9)	135 (87.1)	NE (11.3, NE)	0.8339 (0.4932, 1.4097)	0.4976	0.4962
Negative	40	6 (15.0)	34 (85.0)	NE (9.7, NE)	17	1 (5.9)	16 (94.1)	NE (NE, NE)	1.5311 (0.1739, 13.4822)	0.7011	0.6991

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0371
HER2 IHC 1+	214	28 (13.1)	186 (86.9)	NE (NE, NE)	100	5 (5.0)	95 (95.0)	NE (NE, NE)	2.0683 (0.7922, 5.4002) 0.1378	0.1293	
HER2 IHC 2+/ISH Negative	157	19 (12.1)	138 (87.9)	NE (NE, NE)	72	11 (15.3)	61 (84.7)	NE (NE, NE)	0.6022 (0.2833, 1.2798) 0.1873	0.1844	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.6545
1	220	31 (14.1)	189 (85.9)	NE (NE, NE)	94	9 (9.6)	85 (90.4)	NE (NE, NE)	1.1985 (0.5670, 2.5333) 0.6354	0.6292	
>=2	150	16 (10.7)	134 (89.3)	NE (NE, NE)	78	7 (9.0)	71 (91.0)	NE (8.3, NE)	0.8430 (0.3399, 2.0907) 0.7125	0.7122	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.6985
Yes	233	32 (13.7)	201 (86.3)	NE (NE, NE)	112	10 (8.9)	102 (91.1)	NE (NE, NE)	1.1635 (0.5655, 2.3940) 0.6808	0.6759	
No	98	10 (10.2)	88 (89.8)	NE (NE, NE)	43	4 (9.3)	39 (90.7)	NE (NE, NE)	0.8593 (0.2668, 2.7676) 0.7995	0.7993	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8313
<65	289	37 (12.8)	252 (87.2)	NE (NE, NE)	126	12 (9.5)	114 (90.5)	NE (NE, NE)	1.0143 (0.5236, 1.9649) 0.9664	0.9647	
>=65	82	10 (12.2)	72 (87.8)	NE (NE, NE)	46	4 (8.7)	42 (91.3)	NE (NE, NE)	1.2110 (0.3768, 3.8919) 0.7479	0.7469	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1637
<75	357	45 (12.6)	312 (87.4)	NE (NE, NE)	163	16 (9.8)	147 (90.2)	NE (NE, NE)	0.9746 (0.5461, 1.7392) 0.9306	0.9334	
>=75	14	2 (14.3)	12 (85.7)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9978	0.2525	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.8001
White	175	27 (15.4)	148 (84.6)	NE (NE, NE)	85	9 (10.6)	76 (89.4)	NE (NE, NE)	1.1063 (0.5157, 2.3735) 0.7953	0.7914	
Non-White	196	20 (10.2)	176 (89.8)	NE (NE, NE)	86	7 (8.1)	79 (91.9)	NE (NE, NE)	1.0130 (0.4240, 2.4205) 0.9767	0.9780	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.3952
Asia	147	14 (9.5)	133 (90.5)	NE (NE, NE)	63	6 (9.5)	57 (90.5)	NE (8.3, NE)	0.7579 (0.2867, 2.0033) 0.5762	0.5739	
North America	58	11 (19.0)	47 (81.0)	NE (NE, NE)	28	5 (17.9)	23 (82.1)	NE (NE, NE)	0.7707 (0.2619, 2.2679) 0.6362	0.6392	
Europe + Israel	166	22 (13.3)	144 (86.7)	NE (NE, NE)	81	5 (6.2)	76 (93.8)	NE (NE, NE)	1.7236 (0.6470, 4.5919) 0.2762	0.2700	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											
0	199	17 (8.5)	182 (91.5)	NE (NE, NE)	95	7 (7.4)	88 (92.6)	NE (NE, NE)	0.9252 (0.3807, 2.2487) 0.8638	0.8667	0.5460
1	172	30 (17.4)	142 (82.6)	NE (NE, NE)	77	9 (11.7)	68 (88.3)	NE (8.3, NE)	1.1453 (0.5371, 2.4419) 0.7255	0.7270	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.3457
0	60	9 (15.0)	51 (85.0)	NE (NE, NE)	31	3 (9.7)	28 (90.3)	NE (NE, NE)	1.3406 (0.3603, 4.9879) 0.6619	0.6621	
1	107	17 (15.9)	90 (84.1)	NE (NE, NE)	48	3 (6.3)	45 (93.8)	NE (NE, NE)	2.4255 (0.7097, 8.2892) 0.1576	0.1440	
2	114	13 (11.4)	101 (88.6)	NE (NE, NE)	50	6 (12.0)	44 (88.0)	NE (NE, NE)	0.5779 (0.2121, 1.5749) 0.2837	0.2788	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	8 (8.9)	82 (91.1)	NE (NE, NE)	43	4 (9.3)	39 (90.7)	NE (8.3, NE)	0.6051 (0.1731, 2.1155) 0.4315	0.4289	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.3367
PD	173	16 (9.2)	157 (90.8)	NE (NE, NE)	77	8 (10.4)	69 (89.6)	NE (NE, NE)	0.7056 (0.2976, 1.6732)	0.4269	
PR	48	5 (10.4)	43 (89.6)	NE (NE, NE)	21	2 (9.5)	19 (90.5)	NE (NE, NE)	0.4286 (0.1382, 3.9314)	0.7201	
SD	82	16 (19.5)	66 (80.5)	NE (NE, NE)	54	5 (9.3)	49 (90.7)	NE (8.3, NE)	0.7370 (0.7209, 1.7753)	0.2605	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Reported history of CNS metastases											0.8161
Yes	37	3 (8.1)	34 (91.9)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	1.0250 (0.1066, 9.8588)	0.9829	
No	334	44 (13.2)	290 (86.8)	NE (NE, NE)	159	15 (9.4)	144 (90.6)	NE (NE, NE)	1.0663 (0.5888, 1.9310)	0.8295	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.5011
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9981	0.5892	
No	347	46 (13.3)	301 (86.7)	NE (NE, NE)	165	16 (9.7)	149 (90.3)	NE (NE, NE)	1.0448 (0.5870, 1.8596) 0.8816	0.8778	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.2990
Normal Function	201	26 (12.9)	175 (87.1)	NE (NE, NE)	80	11 (13.8)	69 (86.3)	NE (8.3, NE)	0.7025 (0.3422, 1.4421) 0.3359	0.3356	
Mild Impairment	123	14 (11.4)	109 (88.6)	NE (NE, NE)	65	3 (4.6)	62 (95.4)	NE (NE, NE)	1.9762 (0.5613, 6.9581) 0.2889	0.2790	
Moderate Impairment	41	6 (14.6)	35 (85.4)	NE (NE, NE)	23	2 (8.7)	21 (91.3)	NE (NE, NE)	1.5372 (0.3101, 7.6215) 0.5986	0.5956	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.7702
Normal Function	170	25 (14.7)	145 (85.3)	NE (NE, NE)	88	9 (10.2)	79 (89.8)	NE (NE, NE)	1.0853 (0.5009, 2.3518) 0.8356	0.8368	
Mild Impairment	194	21 (10.8)	173 (89.2)	NE (NE, NE)	82	7 (8.5)	75 (91.5)	NE (NE, NE)	1.0028 (0.4224, 2.3805) 0.9950	0.9912	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.8016
Yes	331	41 (12.4)	290 (87.6)	NE (NE, NE)	146	14 (9.6)	132 (90.4)	NE (NE, NE)	1.0279 (0.5567, 1.8979) 0.9299	0.9262	
No	40	6 (15.0)	34 (85.0)	NE (NE, NE)	26	2 (7.7)	24 (92.3)	NE (NE, NE)	1.2679 (0.2447, 6.5685) 0.7773	0.7768	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.8971
Positive	329	42 (12.8)	287 (87.2)	NE (NE, NE)	152	14 (9.2)	138 (90.8)	NE (NE, NE)	1.0664 (0.5782, 1.9669) 0.8369	0.8333	
Negative	42	5 (11.9)	37 (88.1)	NE (NE, NE)	20	2 (10.0)	18 (90.0)	NE (NE, NE)	0.9824 (0.1866, 5.1724) 0.9832	0.9797	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.7544
Positive	331	42 (12.7)	289 (87.3)	NE (NE, NE)	155	14 (9.0)	141 (91.0)	NE (NE, NE)	1.0834 (0.5873, 1.9984) 0.7977	0.7941	
Negative	40	5 (12.5)	35 (87.5)	NE (NE, NE)	17	2 (11.8)	15 (88.2)	NE (NE, NE)	0.8408 (0.1583, 4.4657) 0.8387	0.8342	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.9285
HER2 IHC 1+	214	27 (12.6)	187 (87.4)	NE (NE, NE)	100	17 (17.0)	83 (83.0)	NE (NE, NE)	0.4008 (0.2127, 0.7551) 0.0047	0.0040	
HER2 IHC 2+/ISH Negative	157	17 (10.8)	140 (89.2)	NE (23.9, NE)	72	12 (16.7)	60 (83.3)	NE (NE, NE)	0.3711 (0.1725, 0.7985) 0.0112	0.0088	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.4188
1	220	20 (9.1)	200 (90.9)	NE (NE, NE)	94	15 (16.0)	79 (84.0)	NE (NE, NE)	0.3613 (0.1809, 0.7217) 0.0039	0.0030	
>=2	150	24 (16.0)	126 (84.0)	23.9 (17.4, NE)	78	14 (17.9)	64 (82.1)	NE (NE, NE)	0.4118 (0.2052, 0.8264) 0.0125	0.0108	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.2312
Yes	233	23 (9.9)	210 (90.1)	NE (NE, NE)	112	12 (10.7)	100 (89.3)	NE (NE, NE)	0.5260 (0.2550, 1.0848) 0.0819	0.0785	
No	98	17 (17.3)	81 (82.7)	NE (19.7, NE)	43	14 (32.6)	29 (67.4)	NE (5.5, NE)	0.3101 (0.1498, 0.6416) 0.0016	0.0012	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3044
<65	289	28 (9.7)	261 (90.3)	NE (NE, NE)	126	19 (15.1)	107 (84.9)	NE (NE, NE)	0.3785 (0.2074, 0.6907) 0.0015	0.0012	
>=65	82	16 (19.5)	66 (80.5)	19.7 (16.2, 23.9)	46	10 (21.7)	36 (78.3)	NE (NE, NE)	0.4562 (0.1959, 1.0623) 0.0688	0.0634	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7183
<75	357	42 (11.8)	315 (88.2)	NE (23.9, NE)	163	27 (16.6)	136 (83.4)	NE (NE, NE)	0.3774 (0.2275, 0.6262) 0.0002	0.0001	
>=75	14	2 (14.3)	12 (85.7)	NE (5.1, NE)	9	2 (22.2)	7 (77.8)	NE (0.0, NE)	0.5373 (0.0753, 3.8331) 0.5355	0.5290	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.0019
White	175	20 (11.4)	155 (88.6)	NE (NE, NE)	85	5 (5.9)	80 (94.1)	NE (NE, NE)	1.0677 (0.3929, 2.9011) 0.8978	0.8983	
Non-White	196	24 (12.2)	172 (87.8)	NE (19.7, NE)	86	24 (27.9)	62 (72.1)	NE (NE, NE)	0.2323 (0.1279, 0.4217) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.0050
Asia	147	18 (12.2)	129 (87.8)	23.9 (19.7, NE)	63	20 (31.7)	43 (68.3)	NE (NE, NE)	0.1870 (0.0949, 0.3685) <0.0001	<0.0001	
North America	58	12 (20.7)	46 (79.3)	NE (11.2, NE)	28	4 (14.3)	24 (85.7)	NE (NE, NE)	0.7116 (0.2163, 2.3414) 0.5756	0.5740	
Europe + Israel	166	14 (8.4)	152 (91.6)	NE (NE, NE)	81	5 (6.2)	76 (93.8)	NE (NE, NE)	0.7966 (0.2802, 2.2644) 0.6697	0.6691	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.4427
0	199	27 (13.6)	172 (86.4)	NE (23.9, NE)	95	15 (15.8)	80 (84.2)	NE (NE, NE)	0.4693 (0.2439, 0.9033) 0.0235	0.0227	
1	172	17 (9.9)	155 (90.1)	NE (NE, NE)	77	14 (18.2)	63 (81.8)	NE (NE, NE)	0.2871 (0.1349, 0.6112) 0.0012	0.0007	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.2044
0	60	6 (10.0)	54 (90.0)	NE (17.4, NE)	31	9 (29.0)	22 (71.0)	NE (2.9, NE)	0.1809 (0.0615, 0.5325) 0.0019	0.0007	
1	107	10 (9.3)	97 (90.7)	NE (NE, NE)	48	9 (18.8)	39 (81.3)	NE (NE, NE)	0.3498 (0.1406, 0.8702) 0.0239	0.0216	
2	114	15 (13.2)	99 (86.8)	NE (NE, NE)	50	6 (12.0)	44 (88.0)	NE (NE, NE)	0.6636 (0.2490, 1.7683) 0.4122	0.4097	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	13 (14.4)	77 (85.6)	23.9 (19.7, NE)	43	5 (11.6)	38 (88.4)	NE (NE, NE)	0.4991 (0.1660, 1.5002) 0.2159	0.2090	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.2086
PD	173	20 (11.6)	153 (88.4)	NE (23.9, NE)	77	10 (13.0)	67 (87.0)	NE (NE, NE)	0.4696 (0.2122, 1.0388)	0.0575	
PR	48	7 (14.6)	41 (85.4)	NE (16.5, NE)	21	7 (33.3)	14 (66.7)	NE (1.5, NE)	0.1583 (0.0475, 0.5274)	0.0008	
SD	82	9 (11.0)	73 (89.0)	NE (19.7, NE)	54	5 (9.3)	49 (90.7)	NE (NE, NE)	0.6500 (0.2065, 2.0459)	0.4676	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.6993
Yes	37	3 (8.1)	34 (91.9)	NE (17.4, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	0.5276 (0.0460, 6.0569)	0.6018	
No	334	41 (12.3)	293 (87.7)	NE (23.9, NE)	159	28 (17.6)	131 (82.4)	NE (NE, NE)	0.3823 (0.2317, 0.6307)	0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.4676
Yes	24	4 (16.7)	20 (83.3)	17.4 (17.4, NE)	7	1 (14.3)	6 (85.7)	NE (0.4, NE)	0.6257 (0.0644, 6.0806) 0.6861	0.6835	
No	347	40 (11.5)	307 (88.5)	NE (23.9, NE)	165	28 (17.0)	137 (83.0)	NE (NE, NE)	0.3731 (0.2253, 0.6179) 0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0417
Normal Function	201	19 (9.5)	182 (90.5)	NE (NE, NE)	80	15 (18.8)	65 (81.3)	NE (NE, NE)	0.2526 (0.1229, 0.5195) 0.0002	<0.0001	
Mild Impairment	123	14 (11.4)	109 (88.6)	23.9 (23.9, NE)	65	9 (13.8)	56 (86.2)	NE (NE, NE)	0.4572 (0.1910, 1.0942) 0.0788	0.0757	
Moderate Impairment	41	11 (26.8)	30 (73.2)	16.2 (9.2, NE)	23	4 (17.4)	19 (82.6)	NE (NE, NE)	1.2888 (0.4096, 4.0545) 0.6644	0.6636	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.6325
Normal Function	170	29 (17.1)	141 (82.9)	23.9 (19.7, NE)	88	19 (21.6)	69 (78.4)	NE (NE, NE)	0.4521 (0.2479, 0.8246) 0.0096	0.0089	
Mild Impairment	194	15 (7.7)	179 (92.3)	NE (NE, NE)	82	10 (12.2)	72 (87.8)	NE (NE, NE)	0.3286 (0.1417, 0.7620) 0.0095	0.0071	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1366
Yes	331	36 (10.9)	295 (89.1)	NE (NE, NE)	146	20 (13.7)	126 (86.3)	NE (NE, NE)	0.4578 (0.2603, 0.8051) 0.0067	0.0059	
No	40	8 (20.0)	32 (80.0)	23.9 (23.9, NE)	26	9 (34.6)	17 (65.4)	NE (2.6, NE)	0.2263 (0.0794, 0.6454) 0.0055	0.0032	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.8062
Positive	329	40 (12.2)	289 (87.8)	NE (NE, NE)	152	26 (17.1)	126 (82.9)	NE (NE, NE)	0.4083 (0.2453, 0.6797)	0.0004	
Negative	42	4 (9.5)	38 (90.5)	23.9 (17.4, 23.9)	20	3 (15.0)	17 (85.0)	NE (3.0, NE)	0.2203 (0.0358, 1.3548)	0.0749	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.6291
Positive	331	40 (12.1)	291 (87.9)	NE (NE, NE)	155	26 (16.8)	129 (83.2)	NE (NE, NE)	0.4149 (0.2492, 0.6910)	0.0006	
Negative	40	4 (10.0)	36 (90.0)	23.9 (17.4, 23.9)	17	3 (17.6)	14 (82.4)	NE (3.0, NE)	0.1653 (0.0261, 1.0469)	0.0319	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.1251
HER2 IHC 1+	214	21 (9.8)	193 (90.2)	NE (NE, NE)	100	13 (13.0)	87 (87.0)	NE (NE, NE)	0.5583 (0.2761, 1.1288) 0.1046	0.1000	
HER2 IHC 2+/ISH Negative	157	22 (14.0)	135 (86.0)	NE (NE, NE)	72	6 (8.3)	66 (91.7)	NE (NE, NE)	1.1091 (0.4444, 2.7680) 0.8244	0.8234	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.0324
1	220	16 (7.3)	204 (92.7)	NE (NE, NE)	94	12 (12.8)	82 (87.2)	NE (NE, NE)	0.4010 (0.1876, 0.8571) 0.0184	0.0148	
>=2	150	26 (17.3)	124 (82.7)	NE (NE, NE)	78	7 (9.0)	71 (91.0)	NE (NE, NE)	1.3842 (0.5936, 3.2279) 0.4517	0.4485	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Vascular disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.8149
Yes	233	29 (12.4)	204 (87.6)	NE (NE, NE)	112	13 (11.6)	99 (88.4)	NE (NE, NE)	0.7243 (0.3715, 1.4123) 0.3438	0.3414	
No	98	8 (8.2)	90 (91.8)	NE (NE, NE)	43	4 (9.3)	39 (90.7)	NE (NE, NE)	0.6394 (0.1893, 2.1592) 0.4713	0.4685	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4161
<65	289	33 (11.4)	256 (88.6)	NE (NE, NE)	126	15 (11.9)	111 (88.1)	NE (NE, NE)	0.6406 (0.3433, 1.1954) 0.1617	0.1593	
>=65	82	10 (12.2)	72 (87.8)	NE (NE, NE)	46	4 (8.7)	42 (91.3)	NE (NE, NE)	1.1455 (0.3572, 3.6738) 0.8193	0.8191	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8576
<75	357	42 (11.8)	315 (88.2)	NE (NE, NE)	163	18 (11.0)	145 (89.0)	NE (NE, NE)	0.7339 (0.4182, 1.2880) 0.2811	0.2798	
>=75	14	1 (7.1)	13 (92.9)	NE (8.4, NE)	9	1 (11.1)	8 (88.9)	NE (0.7, NE)	0.4804 (0.0287, 8.0452) 0.6101	0.6028	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.4549
White	175	26 (14.9)	149 (85.1)	NE (NE, NE)	85	10 (11.8)	75 (88.2)	NE (NE, NE)	0.8682 (0.4137, 1.8221) 0.7086	0.7097	
Non-White	196	17 (8.7)	179 (91.3)	NE (NE, NE)	86	9 (10.5)	77 (89.5)	NE (NE, NE)	0.5837 (0.2564, 1.3291) 0.1997	0.1942	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.7337
Asia	147	7 (4.8)	140 (95.2)	NE (NE, NE)	63	4 (6.3)	59 (93.7)	NE (NE, NE)	0.4214 (0.1176, 1.5098) 0.1844	0.1727	
North America	58	13 (22.4)	45 (77.6)	NE (11.8, NE)	28	6 (21.4)	22 (78.6)	NE (3.7, NE)	0.7511 (0.2790, 2.0223) 0.5712	0.5711	
Europe + Israel	166	23 (13.9)	143 (86.1)	NE (NE, NE)	81	9 (11.1)	72 (88.9)	NE (NE, NE)	0.9117 (0.4183, 1.9873) 0.8162	0.8185	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Vascular disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											
0	199	22 (11.1)	177 (88.9)	NE (NE, NE)	95	11 (11.6)	84 (88.4)	NE (NE, NE)	0.6298 (0.3018, 1.3143) 0.2180	0.2146	0.6017
1	172	21 (12.2)	151 (87.8)	NE (NE, NE)	77	8 (10.4)	69 (89.6)	NE (NE, NE)	0.8703 (0.3791, 1.9978) 0.7432	0.7439	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.0338
0	60	5 (8.3)	55 (91.7)	NE (NE, NE)	31	5 (16.1)	26 (83.9)	NE (NE, NE)	0.4245 (0.1223, 1.4737) 0.1772	0.1667	
1	107	8 (7.5)	99 (92.5)	NE (NE, NE)	48	8 (16.7)	40 (83.3)	NE (NE, NE)	0.3529 (0.1312, 0.9490) 0.0390	0.0312	
2	114	18 (15.8)	96 (84.2)	NE (NE, NE)	50	5 (10.0)	45 (90.0)	NE (NE, NE)	0.9684 (0.3513, 2.6694) 0.9505	0.9493	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Vascular disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	12 (13.3)	78 (86.7)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	3.9266 (0.5029, 30.6597) 0.1921	0.1600	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.3110
PD	173	19 (11.0)	154 (89.0)	NE (NE, NE)	77	9 (11.7)	68 (88.3)	NE (NE, NE)	0.6412 (0.2848, 1.4438)	0.2799	
PR	48	2 (4.2)	46 (95.8)	NE (NE, NE)	21	2 (9.5)	19 (90.5)	NE (NE, NE)	0.2832 (0.0362, 2.1570)	0.1945	
SD	82	13 (15.9)	69 (84.1)	NE (NE, NE)	54	5 (9.3)	49 (90.7)	NE (NE, NE)	0.2215 (1.3131, 0.4636, 3.7191)	0.6070	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Reported history of CNS metastases											0.0764
Yes	37	5 (13.5)	32 (86.5)	NE (11.8, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9962	0.2993	
No	334	38 (11.4)	296 (88.6)	NE (NE, NE)	159	19 (11.9)	140 (88.1)	NE (NE, NE)	0.6679 (0.3812, 1.1702) 0.1584	0.1561	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Vascular disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.6872
Yes	24	2 (8.3)	22 (91.7)	NE (11.4, NE)	7	1 (14.3)	6 (85.7)	NE (0.0, NE)	0.4441 (0.0393, 5.0132) 0.5116	0.5003	
No	347	41 (11.8)	306 (88.2)	NE (NE, NE)	165	18 (10.9)	147 (89.1)	NE (NE, NE)	0.7491 (0.4261, 1.3170) 0.3156	0.3142	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:13; Program name: T4\_AESOCPT10PER\_2\_SAS.sas; Output name: T4\_AESOCPT10PER\_2\_SAS.rtf

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Vascular disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0062
Normal Function	201	19 (9.5)	182 (90.5)	NE (NE, NE)	80	15 (18.8)	65 (81.3)	NE (NE, NE)	0.3394 (0.1695, 0.6795) 0.0023	0.0014	
Mild Impairment	123	17 (13.8)	106 (86.2)	NE (NE, NE)	65	3 (4.6)	62 (95.4)	NE (NE, NE)	1.8474 (0.5311, 6.4264) 0.3345	0.3276	
Moderate Impairment	41	5 (12.2)	36 (87.8)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	2.3267 (0.2712, 19.9651) 0.4413	0.4278	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Vascular disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1479
Normal Function	170	20 (11.8)	150 (88.2)	NE (NE, NE)	88	7 (8.0)	81 (92.0)	NE (NE, NE)	1.0622 (0.4438, 2.5419) 0.8923	0.8931	
Mild Impairment	194	21 (10.8)	173 (89.2)	NE (NE, NE)	82	12 (14.6)	70 (85.4)	NE (NE, NE)	0.4640 (0.2238, 0.9618) 0.0390	0.0351	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Vascular disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.5420
Yes	331	39 (11.8)	292 (88.2)	NE (NE, NE)	146	16 (11.0)	130 (89.0)	NE (NE, NE)	0.7831 (0.4340, 1.4131) 0.4169	0.4159	
No	40	4 (10.0)	36 (90.0)	NE (NE, NE)	26	3 (11.5)	23 (88.5)	NE (NE, NE)	0.4016 (0.0818, 1.9724) 0.2612	0.2502	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Vascular disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.5589
Positive	329	36 (10.9)	293 (89.1)	NE (NE, NE)	152	15 (9.9)	137 (90.1)	NE (NE, NE)	0.7680 (0.4165, 1.4164) 0.3980	0.3962	
Negative	42	7 (16.7)	35 (83.3)	NE (15.5, NE)	20	4 (20.0)	16 (80.0)	NE (2.9, NE)	0.5732 (0.1601, 2.0519) 0.3924	0.3907	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.7.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Vascular disorders; PT: Any PT

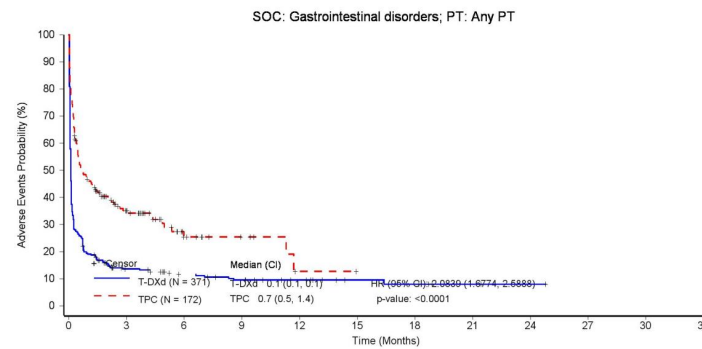
Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.7299
Positive	331	36 (10.9)	295 (89.1)	NE (NE, NE)	155	17 (11.0)	138 (89.0)	NE (NE, NE)	0.7033 (0.3915, 1.2635)	0.2366	
Negative	40	7 (17.5)	33 (82.5)	NE (11.8, NE)	17	2 (11.8)	15 (88.2)	NE (NE, NE)	0.2390 (0.1585, 4.3195)	0.8273	0.8219
									0.8222		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 DE.F.4.7.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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Patients still at risk:

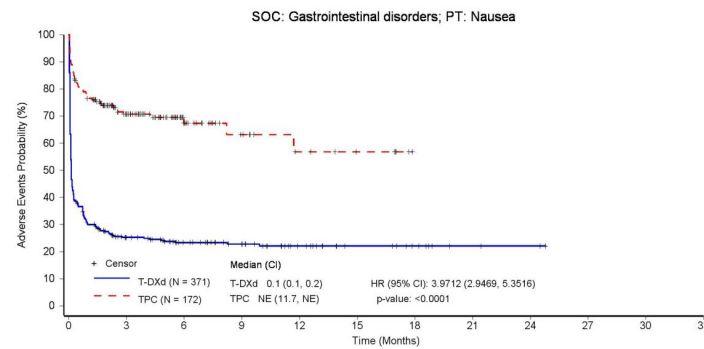
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T-DXd (N = 371)	371	37	24	18	12	6	5	2	1	0	0	0
TPC (N = 172)	172	41	12	6	1	0	0	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 DE.F.4.7.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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Patients still at risk:

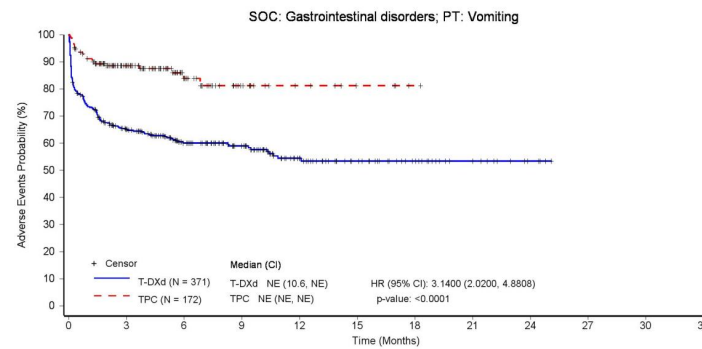
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	73	52	37	22	13	8	3	2	0	0	0
TPC (N = 172)	172	80	30	14	8	5	0	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

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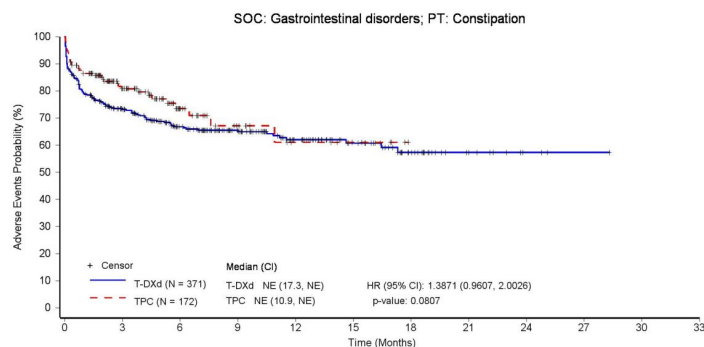
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	205	142	99	54	36	23	11	4	0	0	0
TPC (N = 172)	172	97	39	16	8	4	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

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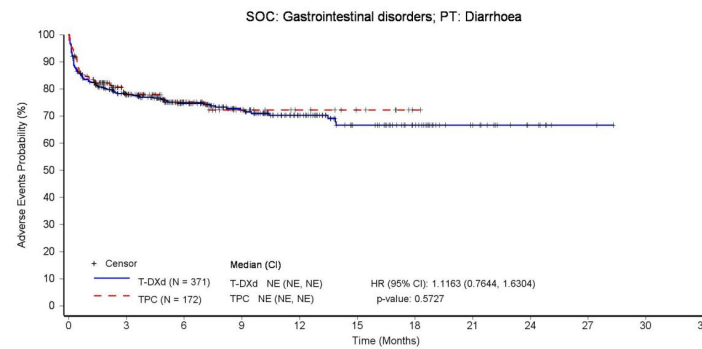
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	225	159	116	74	46	25	9	3	1	0	0
TPC (N = 172)	172	85	31	15	8	5	0	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

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	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	240	175	128	79	49	32	16	7	2	0	0
TPC (N = 172)	172	82	34	18	10	6	1	0	0	0	0	0

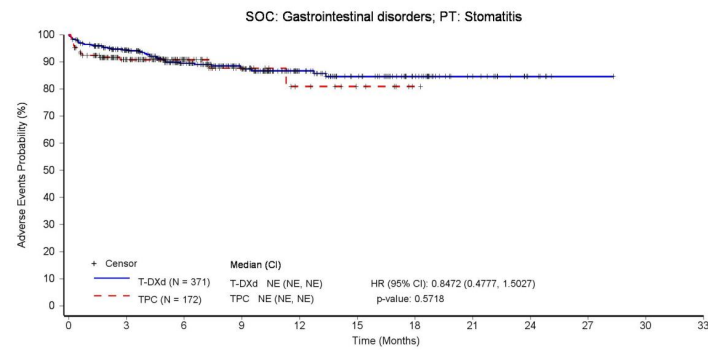
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Patients still at risk:

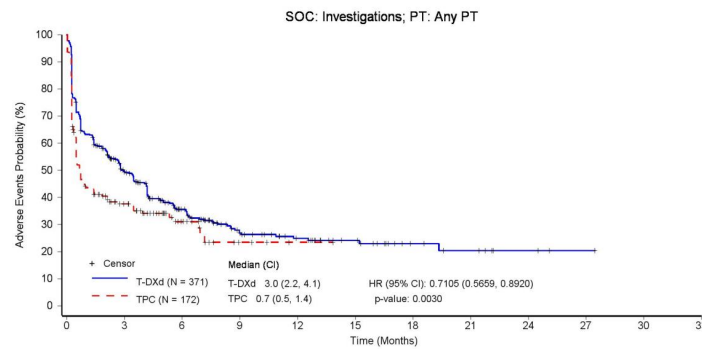
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T-DXd (N = 371)	371	295	210	150	90	63	38	17	6	1	0	0
TPC (N = 172)	172	100	43	20	10	6	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

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Patients still at risk:

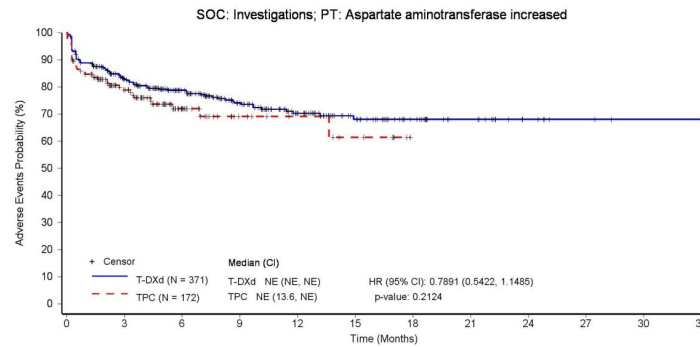
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	161	90	49	33	21	10	7	3	1	0	0
TPC (N = 172)	172	46	17	4	1	0	0	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

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 DE.F.4.7.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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Patients still at risk:

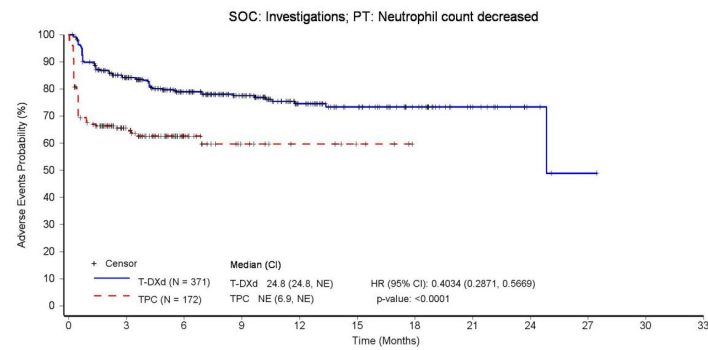
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	265	193	137	88	54	30	17	7	3	1	0
TPC (N = 172)	172	90	34	13	9	6	0	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PER\_3\_SAS.rf

Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.4.7.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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Patients still at risk:

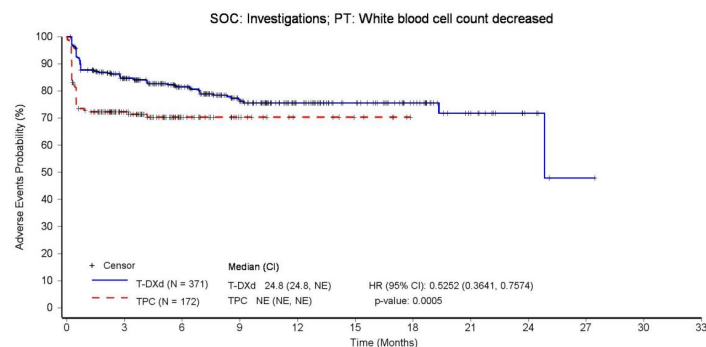
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	266	188	135	79	54	32	13	4	1	0	0
TPC (N = 172)	172	71	27	12	7	4	0	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PER\_3\_SAS.rf

Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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Patients still at risk:

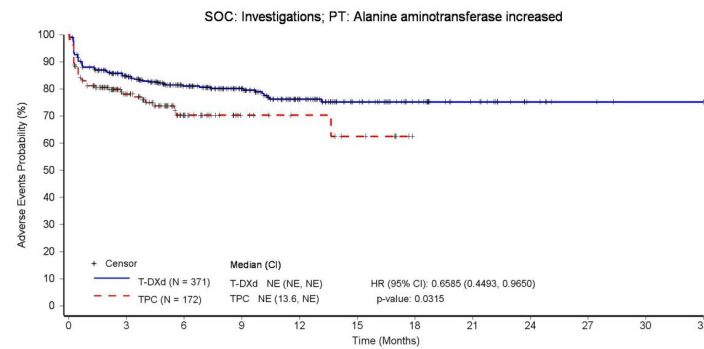
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	266	194	135	84	57	34	14	5	1	0	0
TPC (N = 172)	172	80	33	15	8	5	0	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PER\_3\_SAS.rf

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Patients still at risk:

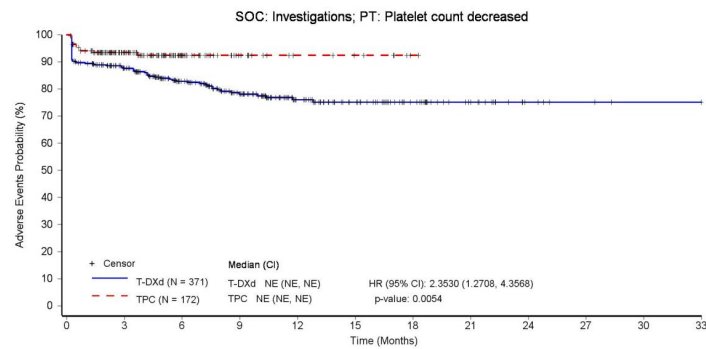
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	267	194	142	87	53	30	18	7	3	1	0
TPC (N = 172)	172	86	33	13	9	6	0	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PER\_3\_SAS.rf

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Patients still at risk:

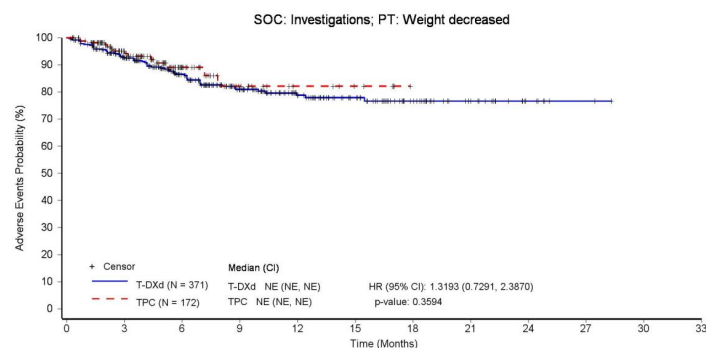
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	277	201	145	90	61	35	17	6	3	1	0
TPC (N = 172)	172	102	41	17	8	6	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PER\_3\_SAS.rf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	291	208	141	94	64	38	19	7	2	0	0
TPC (N = 172)	172	103	41	16	8	5	0	0	0	0	0	0

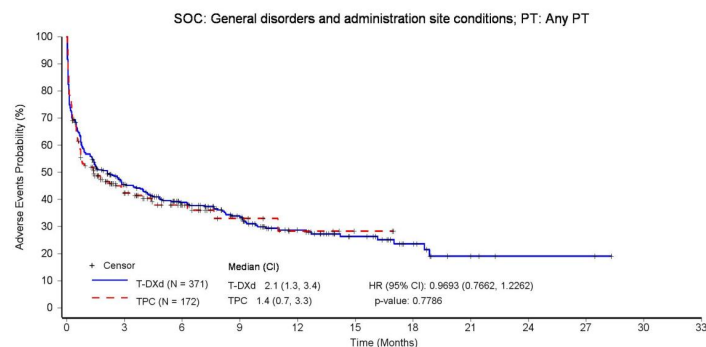
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PER\_3\_SAS.rf



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Patients still at risk:

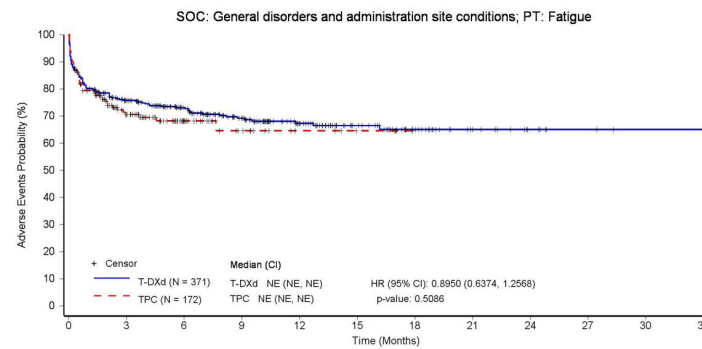
T-DXd (N = 371)	371	145	104	74	42	25	13	4	2	2	0	0
TPC (N = 172)	172	48	22	10	5	2	0	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PER\_3\_SAS.rf

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Patients still at risk:

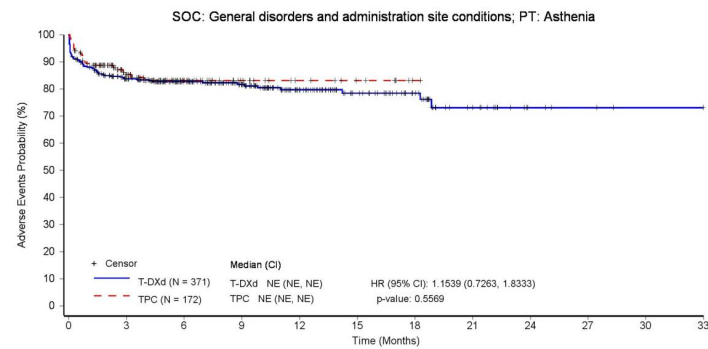
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	239	184	133	85	54	30	14	7	3	1	0
TPC (N = 172)	172	79	33	15	7	4	0	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PER\_3\_SAS.rf

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Patients still at risk:

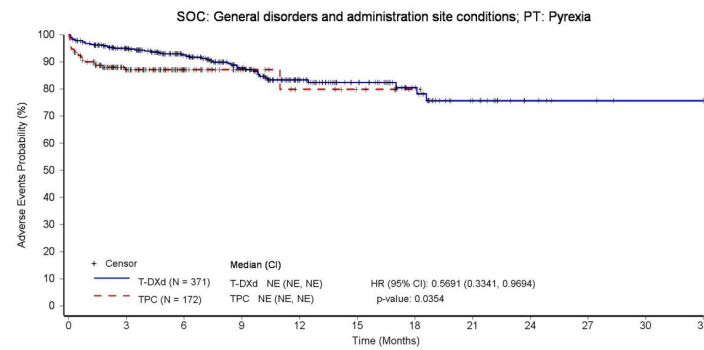
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	261	196	146	90	57	36	16	5	3	1	0
TPC (N = 172)	172	91	39	19	11	7	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PER\_3\_SAS.rf

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Patients still at risk:

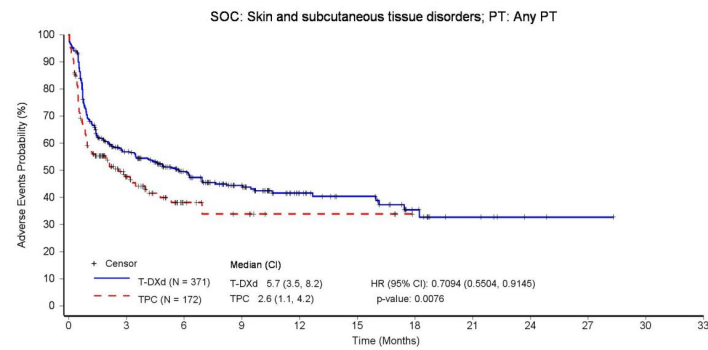
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	300	225	160	93	61	36	16	6	3	1	0
TPC (N = 172)	172	93	41	18	9	6	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PER\_3\_SAS.rf

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Patients still at risk:

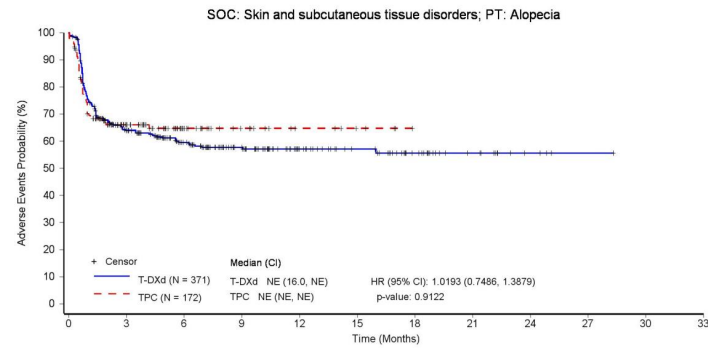
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	173	113	74	38	28	14	6	2	1	0	0
TPC (N = 172)	172	47	12	7	3	3	0	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PER\_3\_SAS.rf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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Patients still at risk:

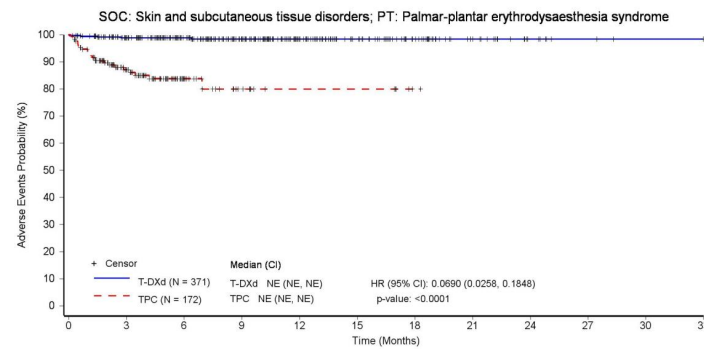
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	196	135	95	56	40	24	12	4	1	0	0
TPC (N = 172)	172	66	28	14	7	4	0	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PER\_3\_SAS.rf

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Patients still at risk:

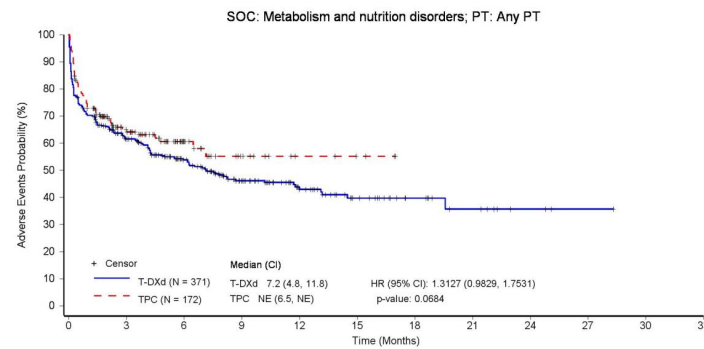
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	310	235	172	110	73	44	20	8	3	1	0
TPC (N = 172)	172	92	31	12	6	6	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PER\_3\_SAS.rf

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 Data Intelligence – Evidence Generation  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	197	131	82	48	28	15	8	3	1	0	0
TPC (N = 172)	172	73	27	12	5	3	0	0	0	0	0	0

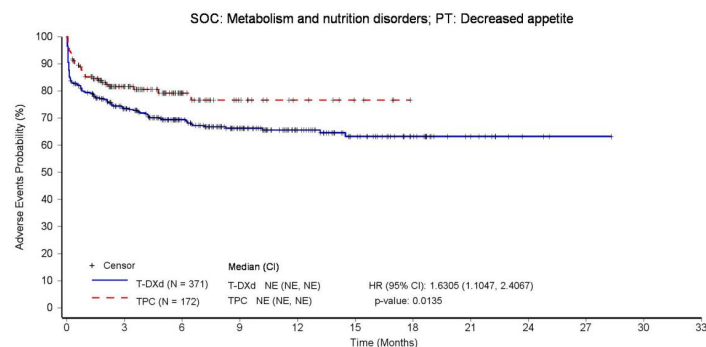
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PER\_3\_SAS.rf



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Patients still at risk:

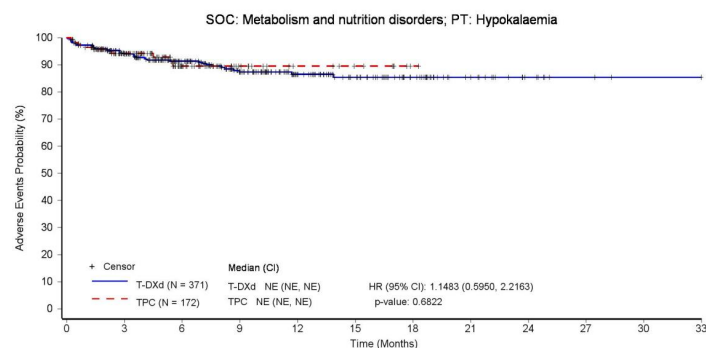
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	229	165	115	71	44	25	10	3	1	0	0
TPC (N = 172)	172	86	34	16	8	4	0	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PER\_3\_SAS.rf

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Patients still at risk:

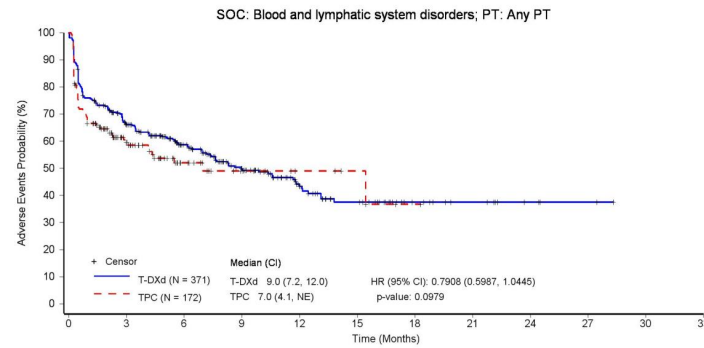
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	296	220	155	97	66	38	18	8	3	1	0
TPC (N = 172)	172	102	40	18	10	7	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PER\_3\_SAS.rf

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Patients still at risk:

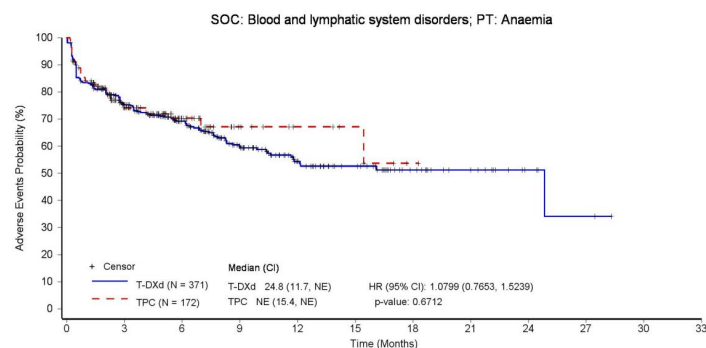
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T-DXd (N = 371)	371	216	143	92	50	31	14	9	4	2	0	0
TPC (N = 172)	172	61	24	11	6	4	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

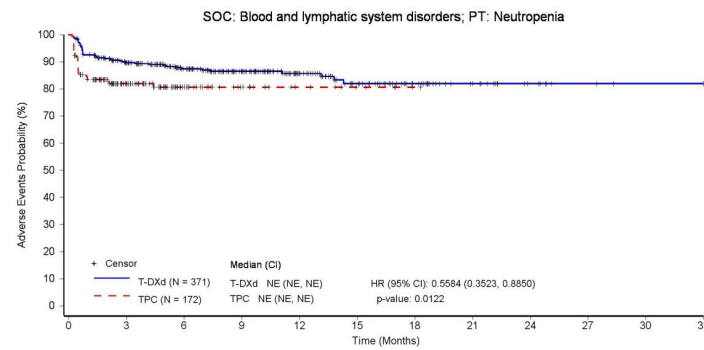
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	241	170	111	65	45	23	13	5	2	0	0
TPC (N = 172)	172	79	33	12	7	5	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PER\_3\_SAS.rf

Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.4.7.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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Patients still at risk:

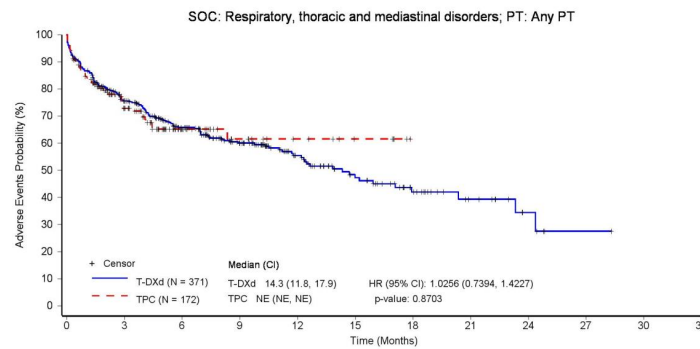
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	281	204	147	89	55	33	17	8	3	1	0
TPC (N = 172)	172	85	36	17	9	5	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PER\_3\_SAS.rf

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Patients still at risk:

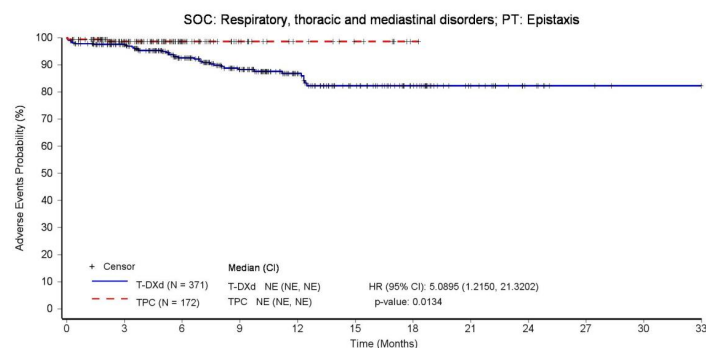
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	250	176	125	73	43	25	13	5	1	0	0
TPC (N = 172)	172	81	33	15	9	5	0	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PER\_3\_SAS.rf

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Patients still at risk:

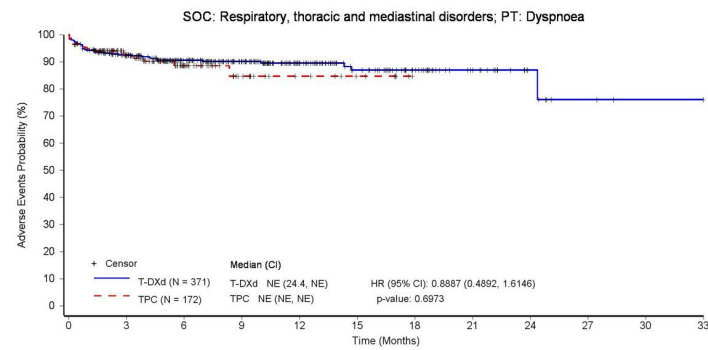
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	309	222	158	99	64	39	18	8	3	1	0
TPC (N = 172)	172	105	44	20	11	7	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PER\_3\_SAS.rf

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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	299	225	165	104	66	41	20	8	3	1	0
TPC (N = 172)	172	101	41	18	10	6	0	0	0	0	0	0

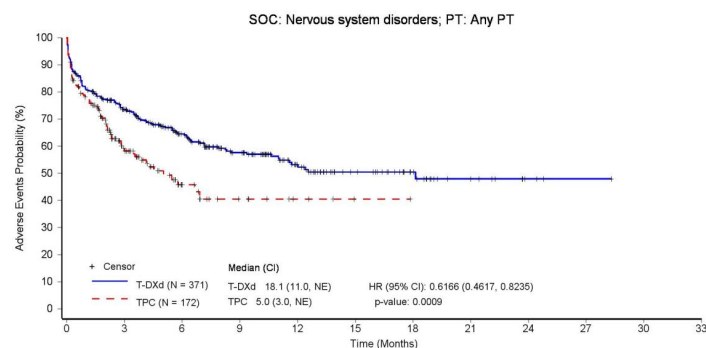
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PER\_3\_SAS.rf



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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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Patients still at risk:

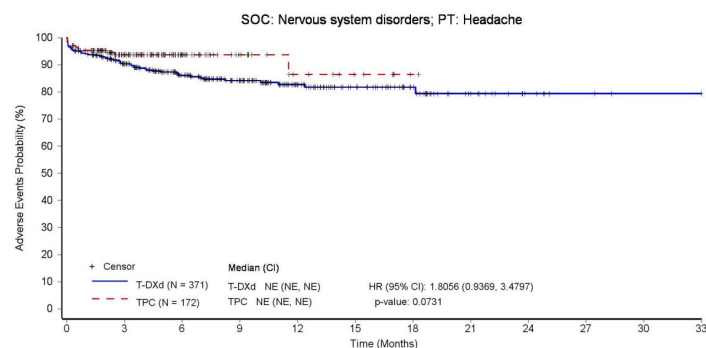
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	231	155	104	60	35	21	9	3	1	0	0
TPC (N = 172)	172	61	20	9	4	1	0	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PER\_3\_SAS.rf

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Patients still at risk:

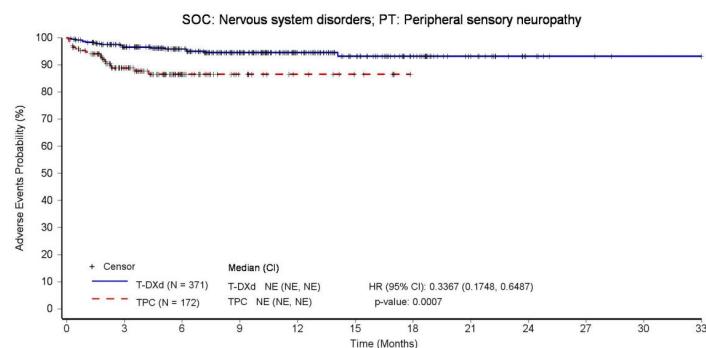
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	282	201	144	89	59	36	16	7	3	1	0
TPC (N = 172)	172	100	41	19	10	6	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PER\_3\_SAS.rf

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Patients still at risk:

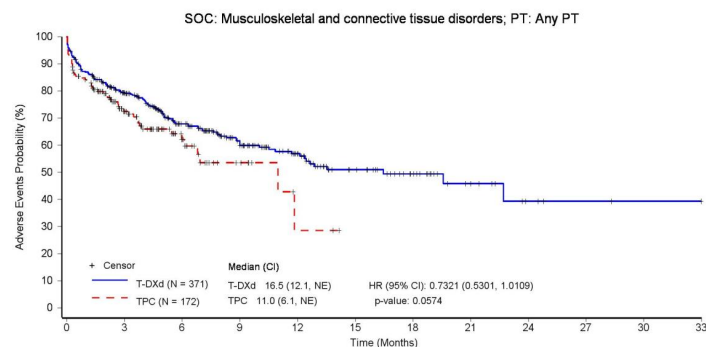
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	303	228	165	102	66	39	19	7	3	1	0
TPC (N = 172)	172	94	37	17	9	5	0	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 Data Intelligence – Evidence Generation  
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Patients still at risk:

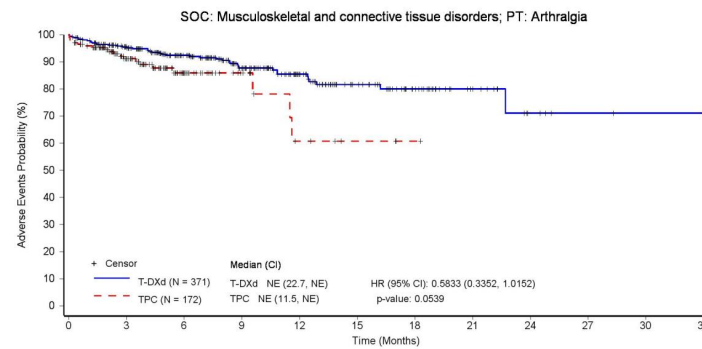
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	250	166	107	65	39	23	10	4	2	1	0
TPC (N = 172)	172	77	28	9	2	0	0	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PER\_3\_SAS.rf

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Patients still at risk:

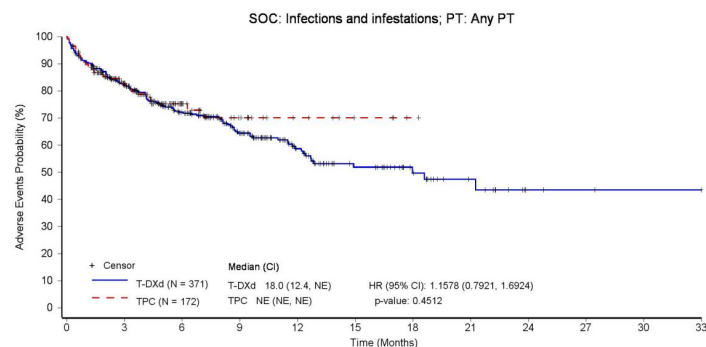
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	300	220	153	95	59	34	14	5	2	1	0
TPC (N = 172)	172	172	98	35	15	6	3	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PER\_3\_SAS.rf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
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Patients still at risk:

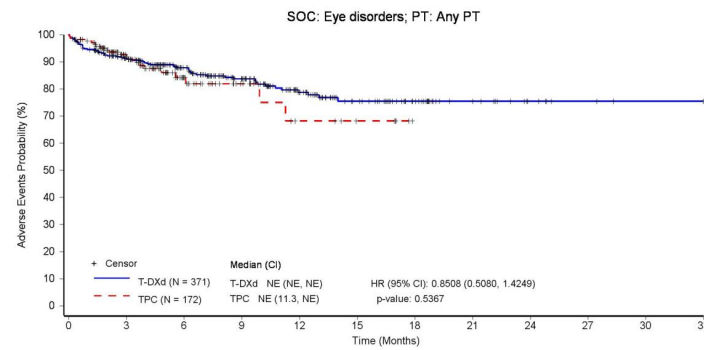
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	263	184	120	67	40	23	12	3	2	1	0
TPC (N = 172)	172	90	35	16	8	4	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PER\_3\_SAS.rf

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Patients still at risk:

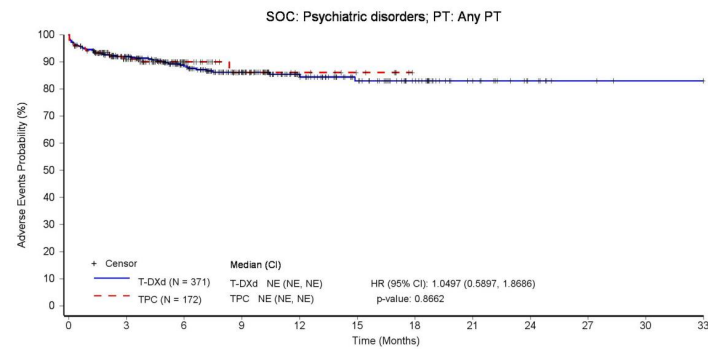
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	285	211	149	89	54	32	15	7	3	1	0
TPC (N = 172)	172	98	38	17	8	5	0	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PER\_3\_SAS.rf

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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	292	209	147	86	58	35	17	8	3	1	0
TPC (N = 172)	172	96	39	18	10	6	0	0	0	0	0	0

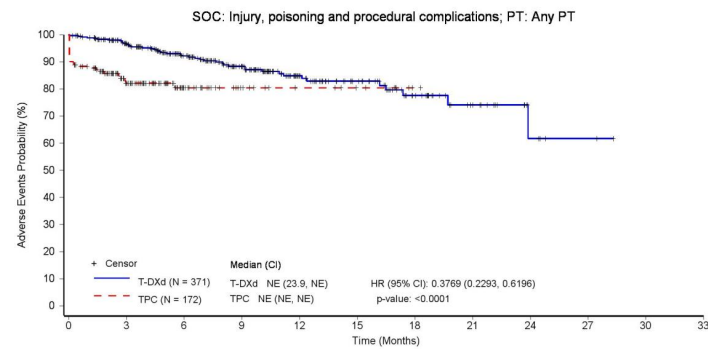
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PER\_3\_SAS.rf



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Patients still at risk:

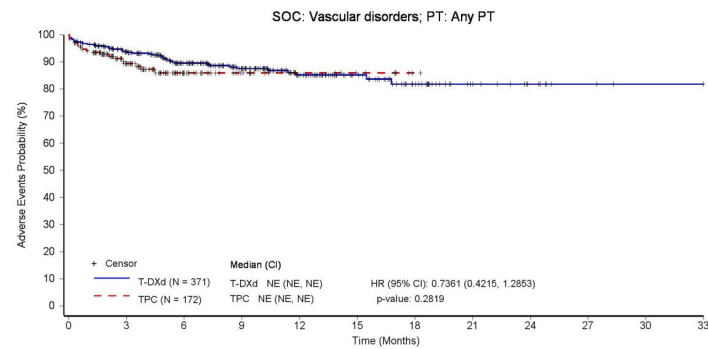
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	304	218	153	89	61	34	16	5	2	0	0
TPC (N = 172)	172	86	34	16	10	7	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PER\_3\_SAS.rf

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Patients still at risk:

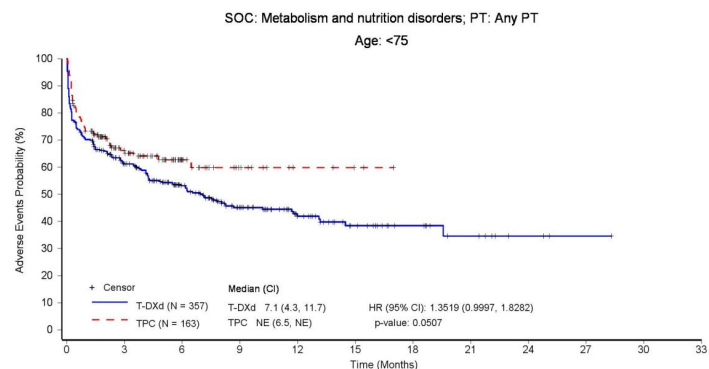
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	298	215	155	95	60	34	14	8	3	1	0
TPC (N = 172)	172	96	40	19	10	7	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:13; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PER\_3\_SAS.rf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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 DE.F.4.7.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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Patients still at risk:

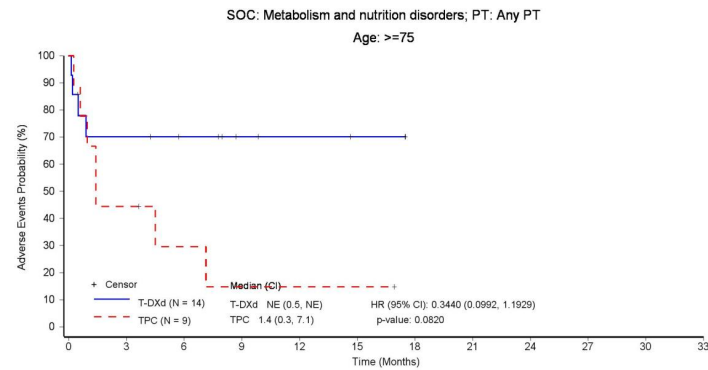
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 357)	357	188	124	78	45	26	15	8	3	1	0	0
TPC (N = 163)	163	69	25	11	4	2	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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Patients still at risk:

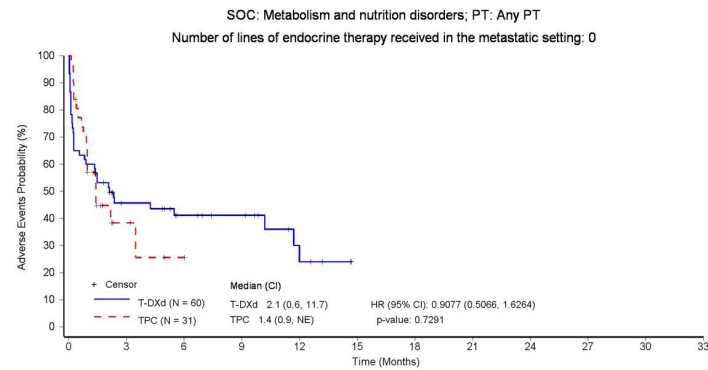
T-DXd (N = 14)	14	9	7	4	3	2	0	0	0	0	0	0
TPC (N = 9)	9	4	2	1	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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Patients still at risk:

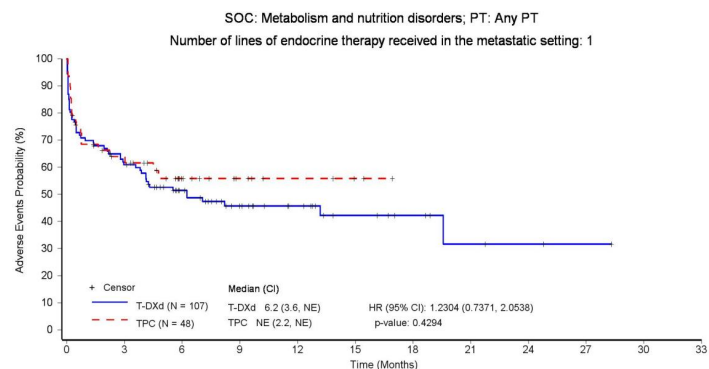
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 60)	60	22	14	11	4	0	0	0	0	0	0	0
TPC (N = 31)	31	4	1	0	0	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.4.7.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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Patients still at risk:

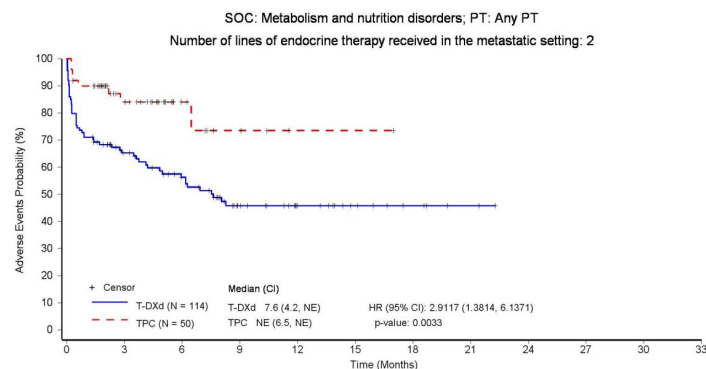
T-DXd (N = 107)	107	60	39	25	17	10	6	3	2	1	0	0
TPC (N = 48)	48	27	13	7	4	2	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.4.7.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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Patients still at risk:

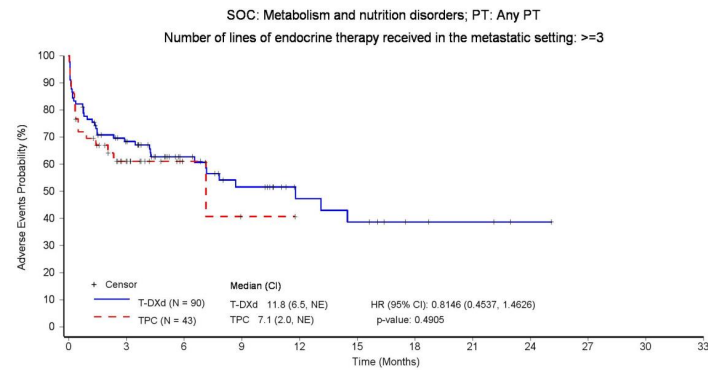
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 114)	114	61	46	26	16	9	5	2	0	0	0	0
TPC (N = 50)	50	27	9	4	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 90)	90	54	32	20	11	9	4	3	1	0	0	0
TPC (N = 43)	43	15	4	1	0	0	0	0	0	0	0	0

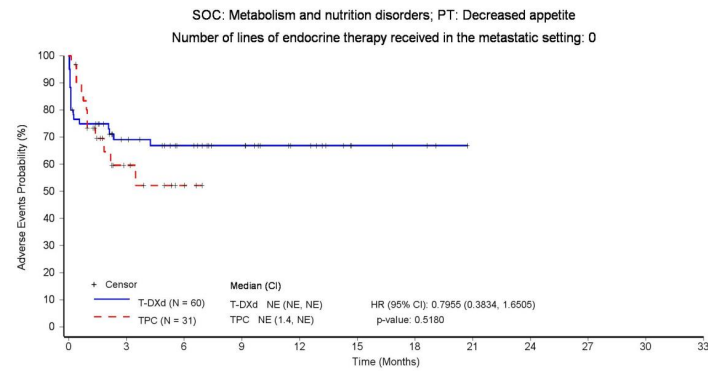
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf



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Patients still at risk:

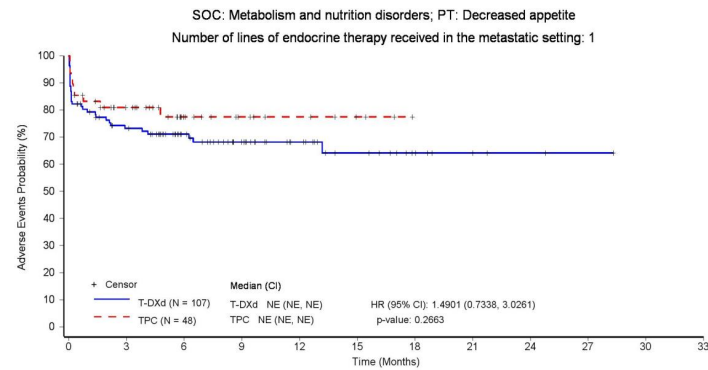
T-DXd (N = 60)	60	33	24	18	11	4	3	0	0	0	0	0
TPC (N = 31)	31	9	3	0	0	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

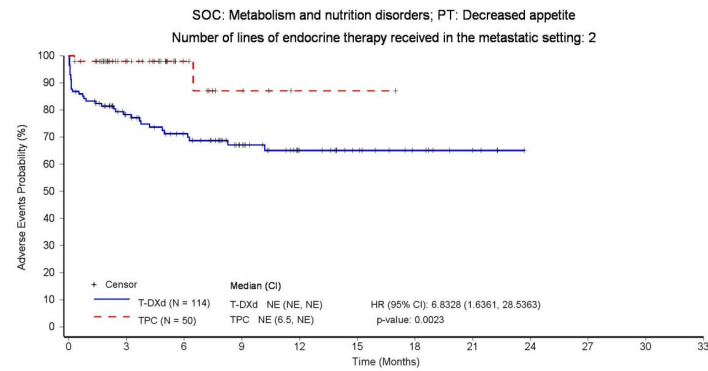
T-DXd (N = 107)	107	70	50	34	22	14	7	3	2	1	0	0
TPC (N = 48)	48	30	15	9	6	3	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

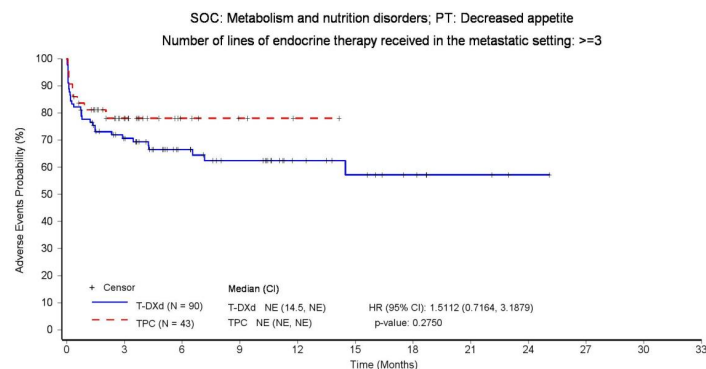
T-DXd (N = 114)	114	70	56	38	23	15	9	4	0	0	0	0
TPC (N = 50)	50	29	10	4	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

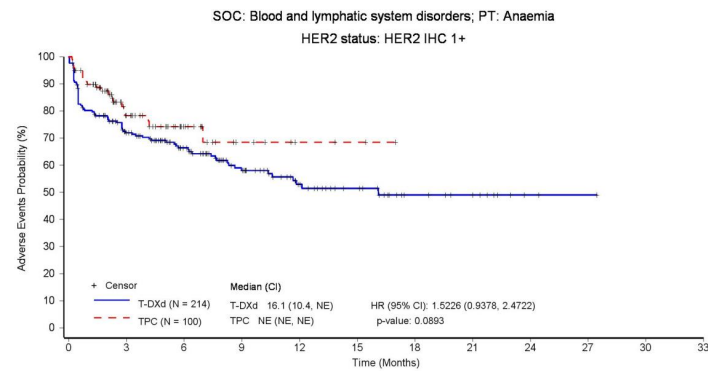
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 90)	90	56	35	25	15	11	6	3	1	0	0	0
TPC (N = 43)	43	18	6	3	1	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

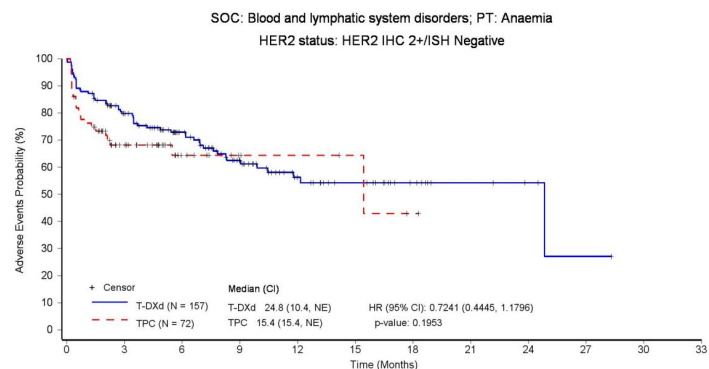
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 214)	214	131	93	62	37	26	13	8	2	1	0	0
TPC (N = 100)	100	45	21	7	3	2	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

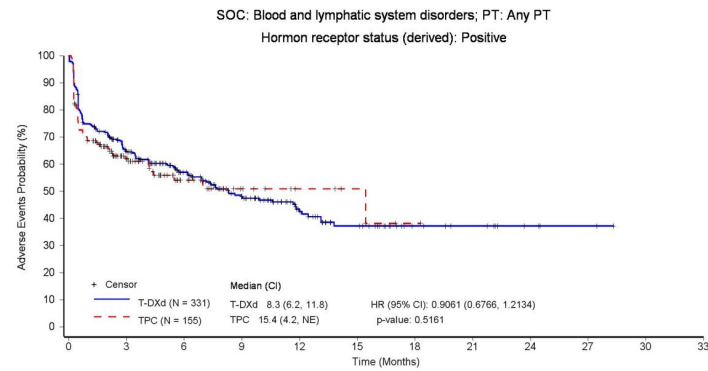
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 157)	157	110	77	49	28	19	10	5	3	1	0	0
TPC (N = 72)	72	34	12	5	4	3	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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Patients still at risk:

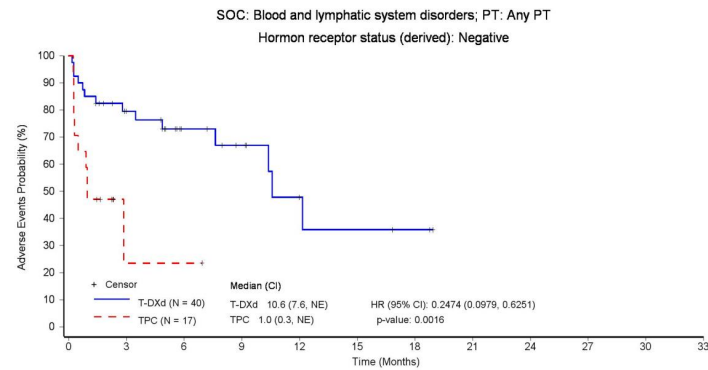
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 331)	331	191	130	83	46	28	12	9	4	2	0	0
TPC (N = 155)	155	60	23	11	6	4	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 40)	40	25	13	9	4	3	2	0	0	0	0	0
TPC (N = 17)	17	1	1	0	0	0	0	0	0	0	0	0

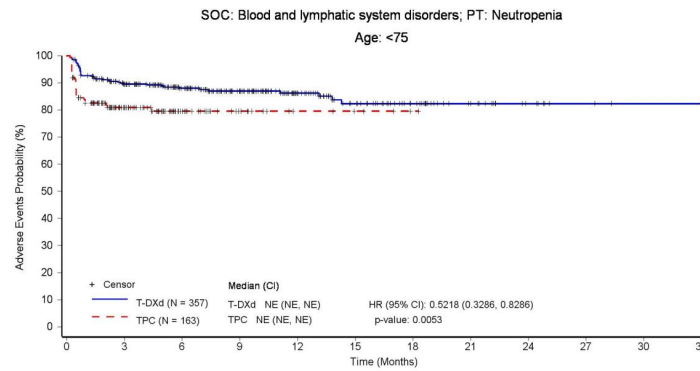
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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 DE.F.4.7.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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Patients still at risk:

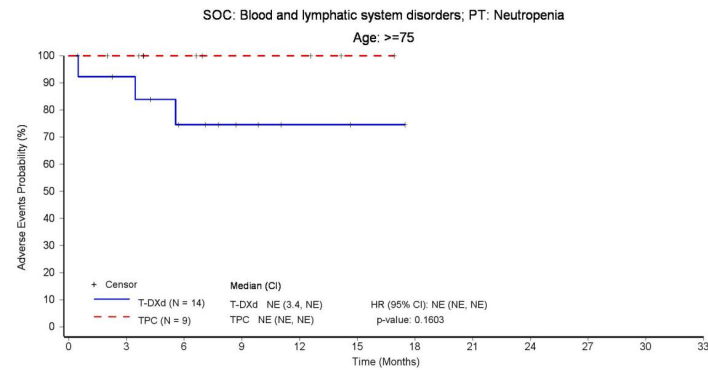
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 357)	357	270	197	143	87	54	33	17	8	3	1	0
TPC (N = 163)	163	77	31	14	6	4	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

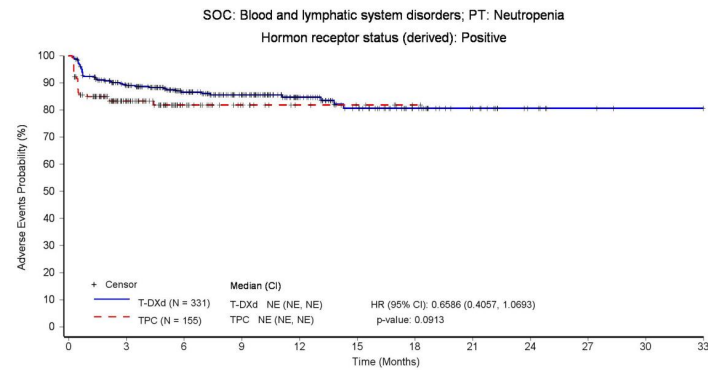
T-DXd (N = 14)	14	11	7	4	2	1	0	0	0	0	0
TPC (N = 9)	9	8	5	3	3	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

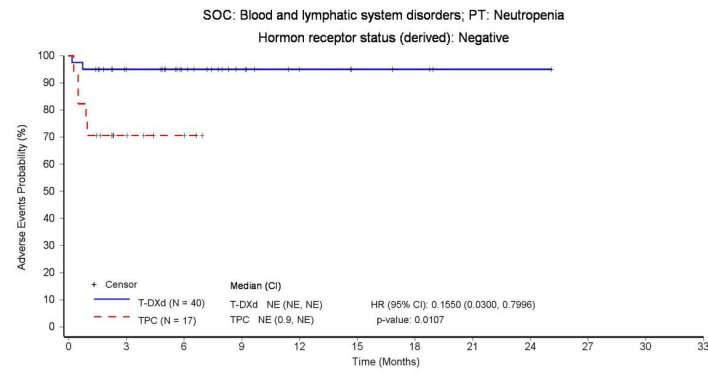
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 331)	331	252	185	136	83	51	30	16	7	3	1	0
TPC (N = 155)	155	79	33	17	9	5	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

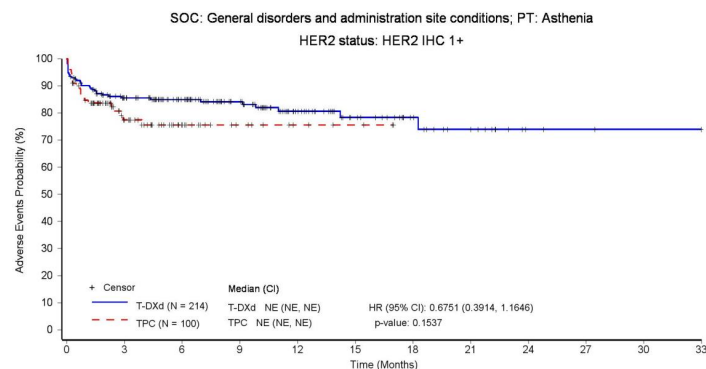
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 40)	40	29	19	11	6	4	3	1	1	0	0	0
TPC (N = 17)	17	6	3	0	0	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

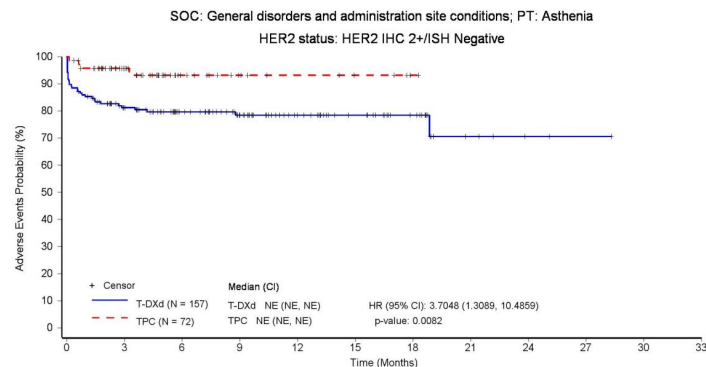
T-DXd (N = 214)	214	152	116	86	51	30	19	11	3	2	1	0
TPC (N = 100)	100	46	22	10	5	3	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

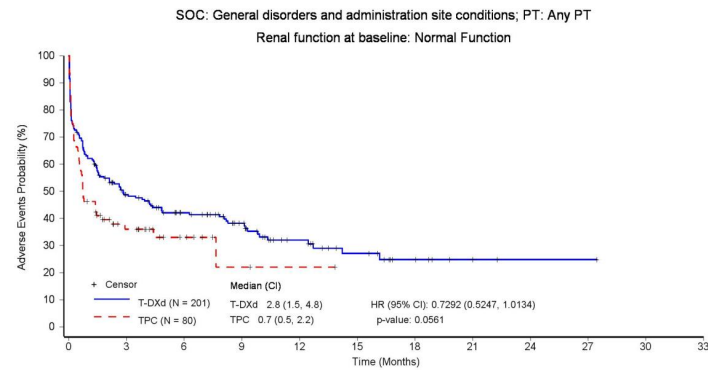
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 157)	157	109	80	60	39	27	17	5	2	1	0	0
TPC (N = 72)	72	45	17	9	6	4	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

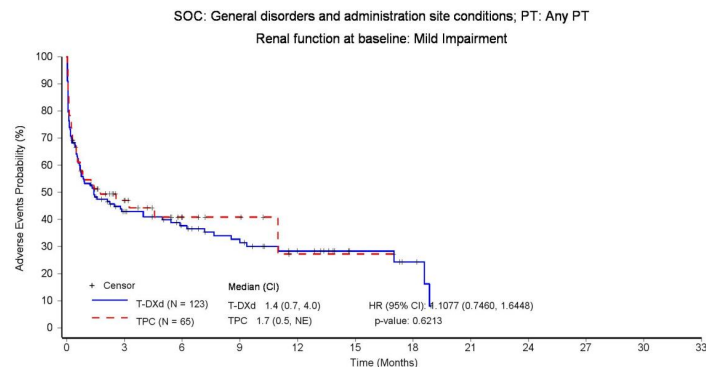
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 201)	201	84	61	43	23	14	7	2	1	1	0	0
TPC (N = 80)	80	19	8	2	1	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.4.7.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 123)	123	45	33	25	15	7	4	0	0	0	0	0
TPC (N = 65)	65	19	8	5	1	1	0	0	0	0	0	0

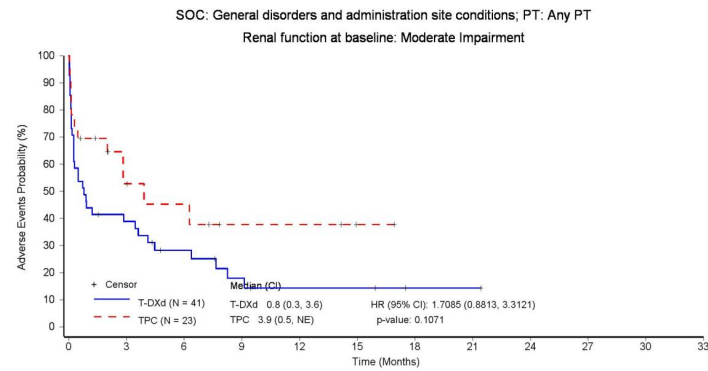
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf



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Patients still at risk:

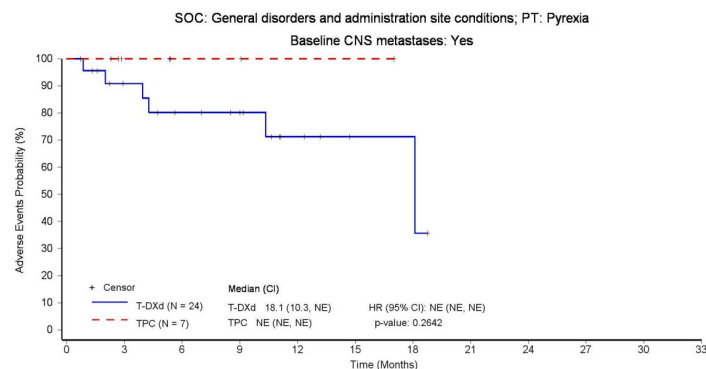
T-DXd (N = 41)	41	15	9	5	3	3	1	1	0	0	0	0
TPC (N = 23)	23	9	6	3	3	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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Patients still at risk:

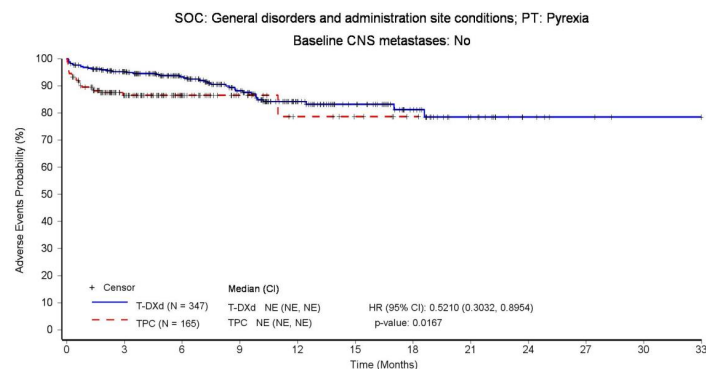
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 24)	24	17	13	11	5	2	2	0	0	0	0	0
TPC (N = 7)	7	4	2	2	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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Patients still at risk:

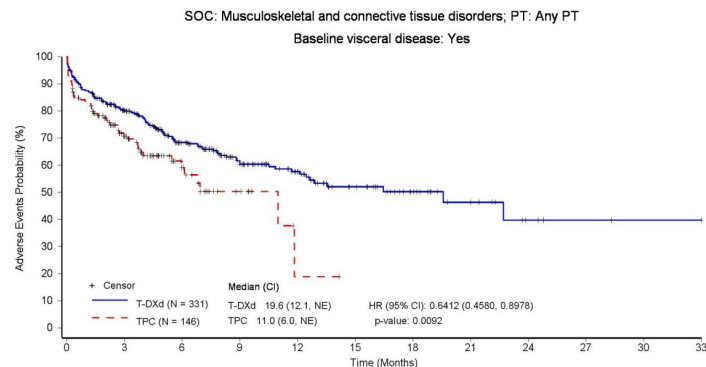
T-DXd (N = 347)	347	283	212	149	88	59	34	16	6	3	1	0
TPC (N = 165)	165	89	39	16	8	5	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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Patients still at risk:

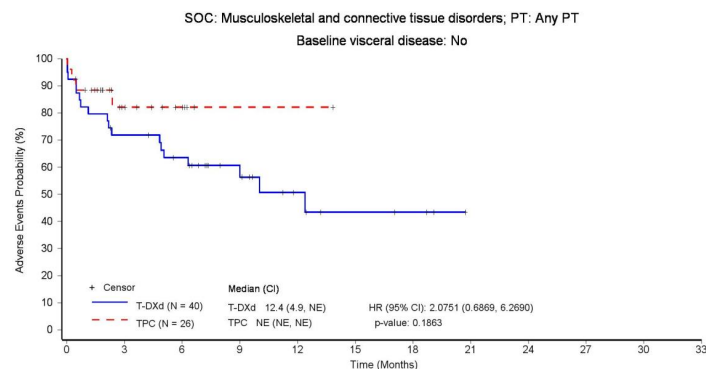
T-DXd (N = 331)	331	223	144	93	58	35	20	10	4	2	1	0
TPC (N = 146)	146	66	23	8	1	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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Patients still at risk:

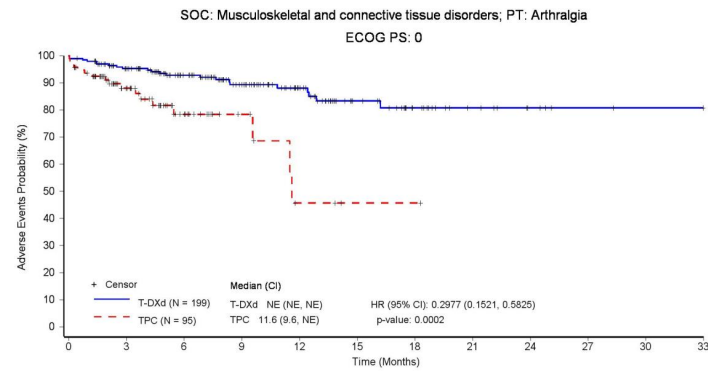
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 40)	40	27	22	14	7	4	3	0	0	0	0	0
TPC (N = 26)	26	11	5	1	1	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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Patients still at risk:

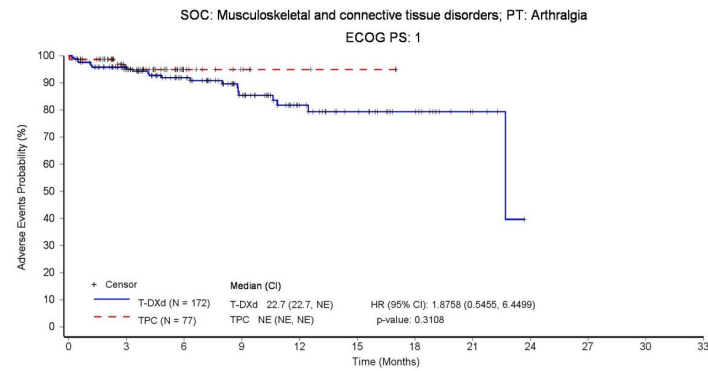
T-DXd (N = 199)	199	170	128	93	60	36	20	10	5	2	1	0
TPC (N = 95)	95	51	21	9	3	1	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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Patients still at risk:

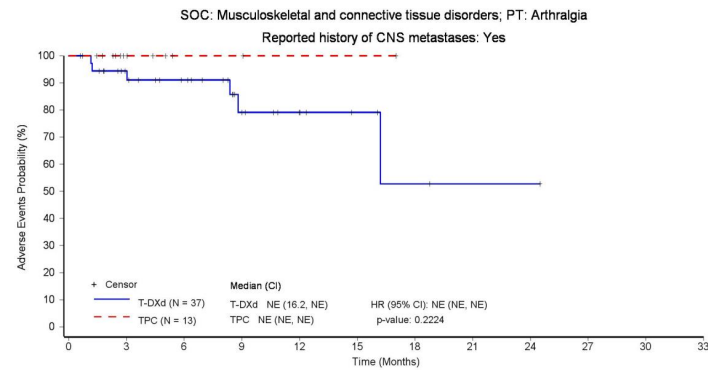
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 172)	172	130	92	60	35	23	14	4	0	0	0	0
TPC (N = 77)	77	47	14	6	3	2	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

T-DXd (N = 37)	37	28	22	12	7	4	2	1	1	0	0	0
TPC (N = 13)	13	6	2	2	1	1	0	0	0	0	0	0

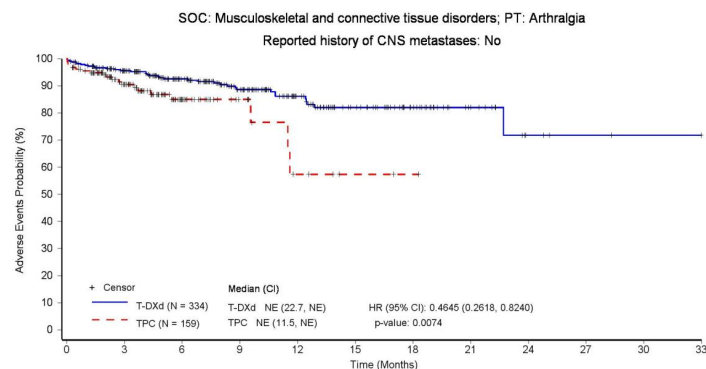
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf



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Patients still at risk:

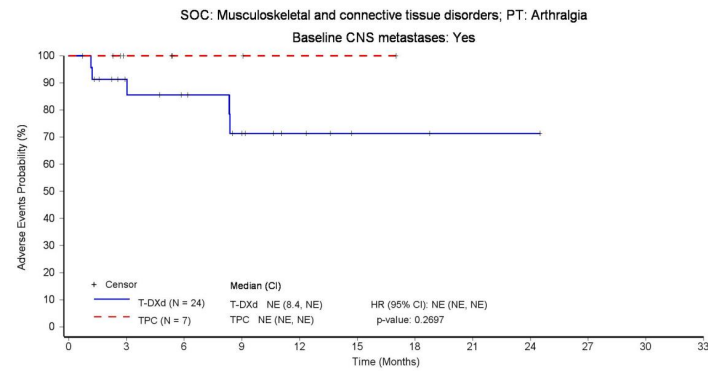
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 334)	334	272	198	141	88	55	32	13	4	2	1	0
TPC (N = 159)	159	92	33	13	5	2	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

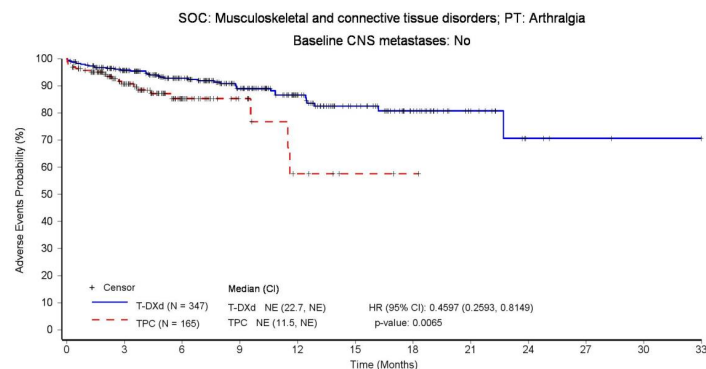
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 24)	24	16	13	9	5	2	2	1	1	0	0	0
TPC (N = 7)	7	4	2	2	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

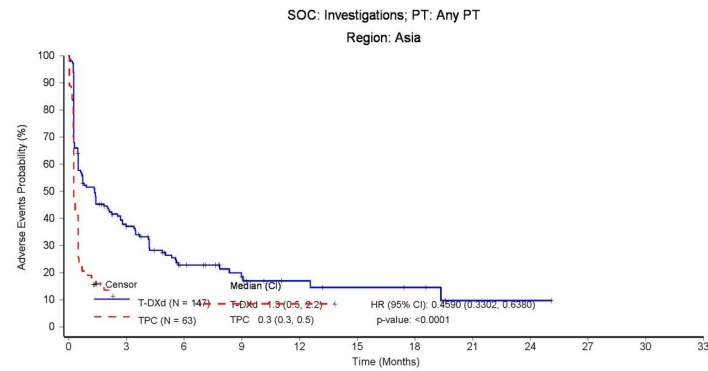
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 347)	347	284	207	144	90	57	32	13	4	2	1	0
TPC (N = 165)	165	94	33	13	5	2	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

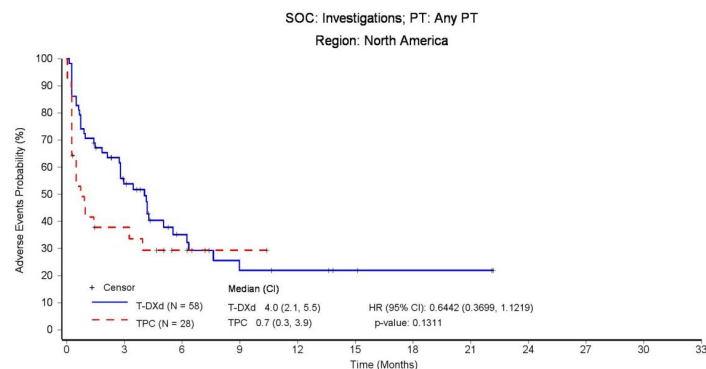
T-DXd (N = 147)	147	48	22	13	7	5	4	1	1	0	0	0
TPC (N = 63)	63	4	3	1	1	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

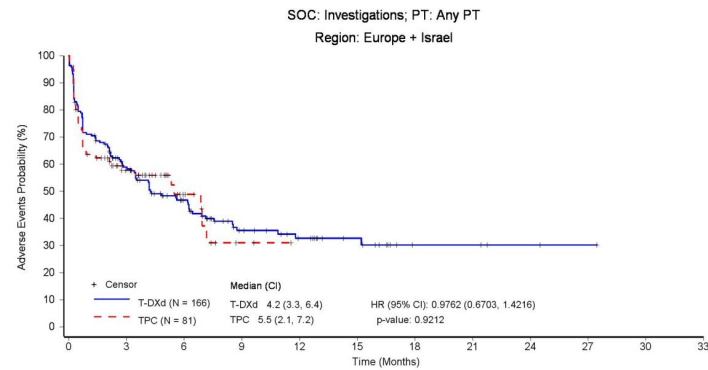
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 58)	58	27	12	6	5	3	2	2	0	0	0	0
TPC (N = 28)	28	9	3	1	0	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

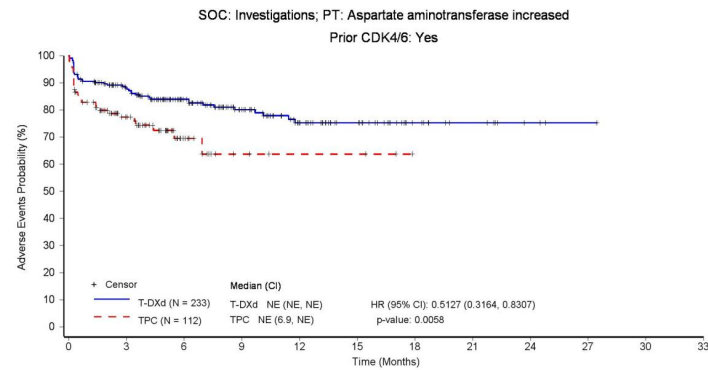
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 166)	166	86	56	30	21	13	4	4	2	1	0	0
TPC (N = 81)	81	33	11	2	0	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

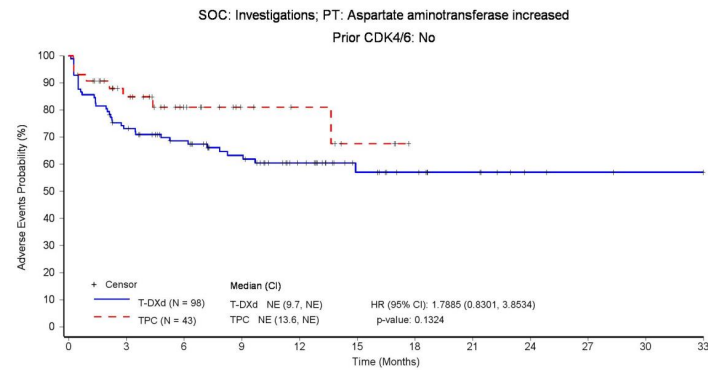
T-DXd (N = 233)	233	173	121	82	52	34	15	8	3	1	0	0
TPC (N = 112)	112	56	17	5	3	3	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 98)	98	69	57	45	30	17	12	8	3	2	1	0
TPC (N = 43)	43	28	15	8	6	3	0	0	0	0	0	0

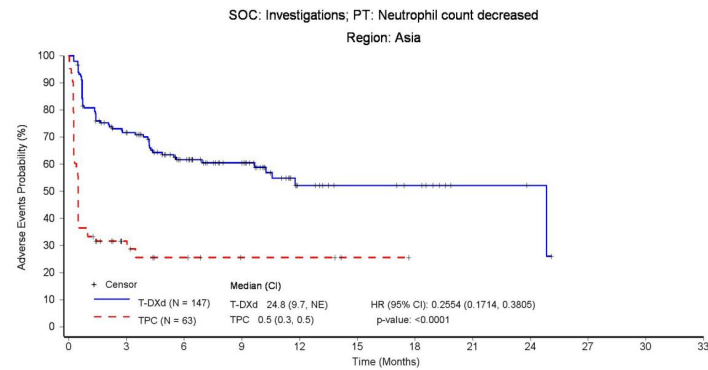
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Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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 DE.F.4.7.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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Patients still at risk:

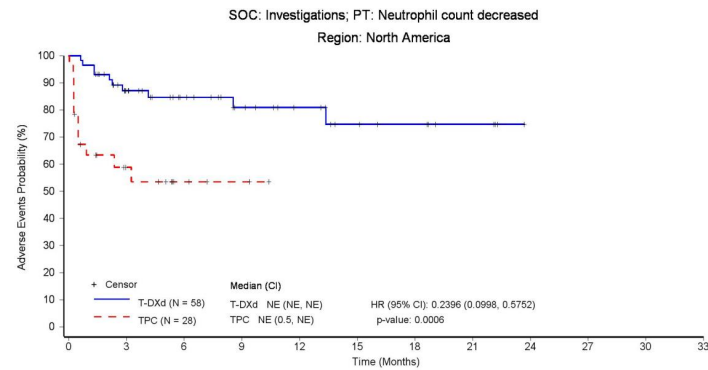
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 147)	147	95	60	44	16	11	9	3	2	0	0	0
TPC (N = 63)	63	11	6	3	3	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.4.7.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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Patients still at risk:

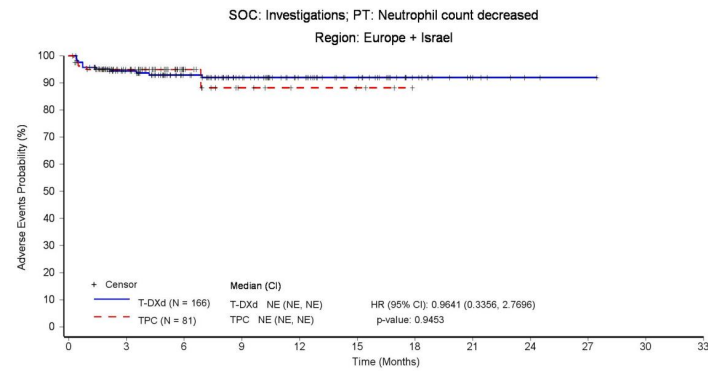
T-DXd (N = 58)	58	39	28	20	15	9	7	4	0	0	0	0
TPC (N = 28)	28	11	4	2	0	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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 Data Intelligence – Evidence Generation  
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 D.E.F.4.7.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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Patients still at risk:

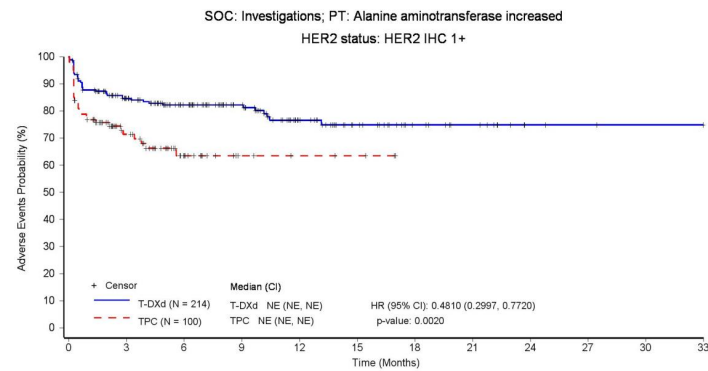
T-DXd (N = 166)	166	132	100	71	48	34	16	6	2	1	0	0
TPC (N = 81)	81	49	17	7	4	3	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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Patients still at risk:

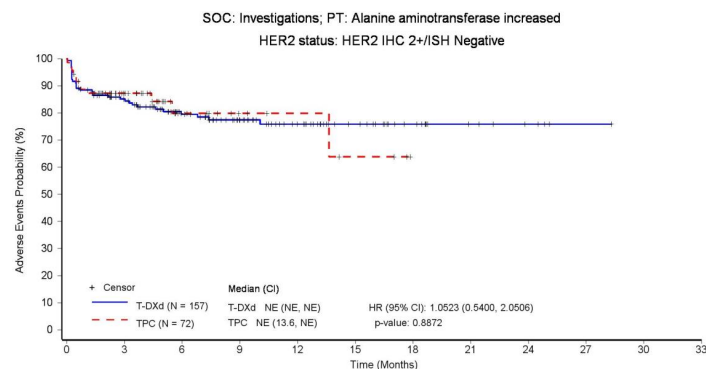
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 214)	214	150	113	85	49	29	16	11	3	2	1	0
TPC (N = 100)	100	46	20	6	4	3	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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Patients still at risk:

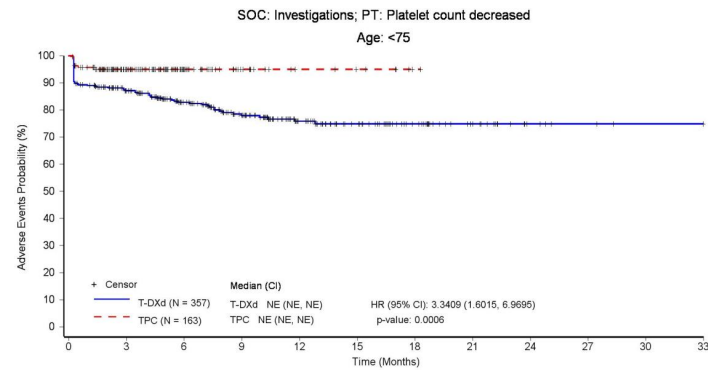
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 157)	157	117	81	57	38	24	14	7	4	1	0	0
TPC (N = 72)	72	40	13	7	5	3	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

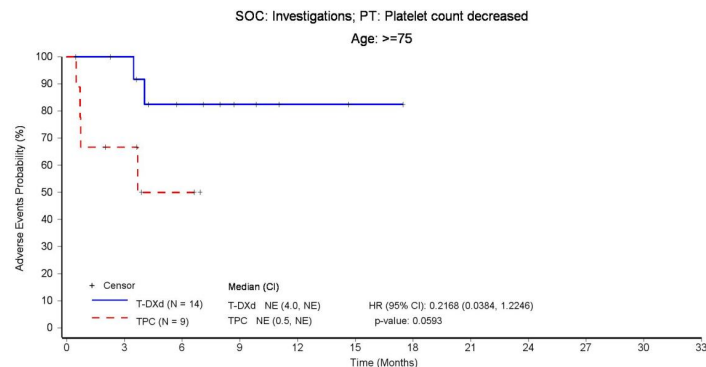
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 357)	357	265	194	141	88	60	35	17	6	3	1	0
TPC (N = 163)	163	97	39	17	8	6	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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Patients still at risk:

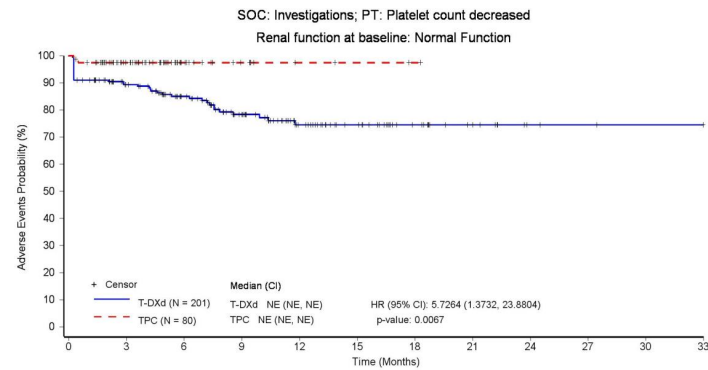
T-DXd (N = 14)	14	12	7	4	2	1	0	0	0	0	0
TPC (N = 9)	9	5	2	0	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 201)	201	155	113	80	47	33	18	9	3	2	1	0
TPC (N = 80)	80	49	18	8	3	2	1	0	0	0	0	0

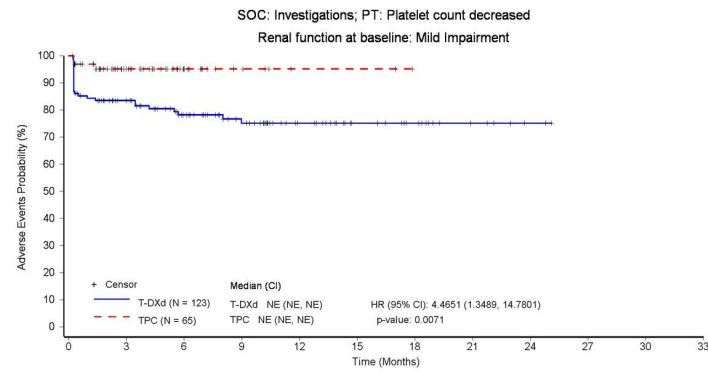
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf



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Patients still at risk:

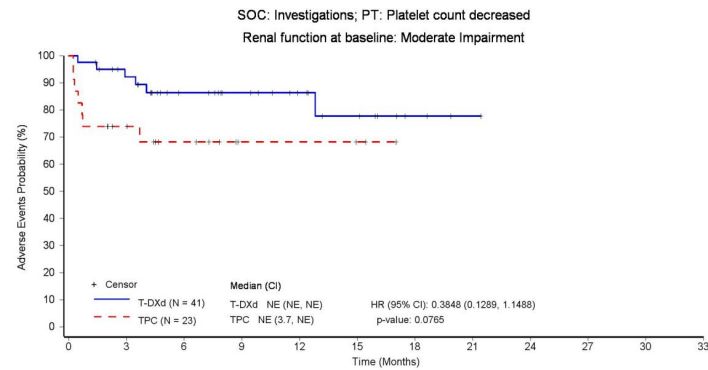
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 123)	123	86	64	47	30	19	13	6	2	0	0	0
TPC (N = 65)	65	37	15	6	2	2	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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Patients still at risk:

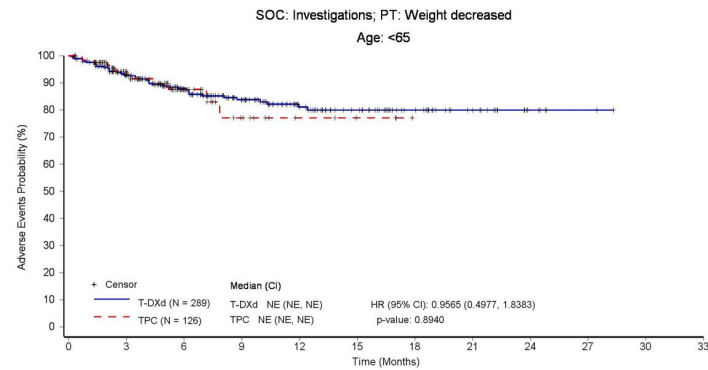
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 41)	41	33	22	17	12	8	3	1	0	0	0	0
TPC (N = 23)	23	14	8	3	3	2	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

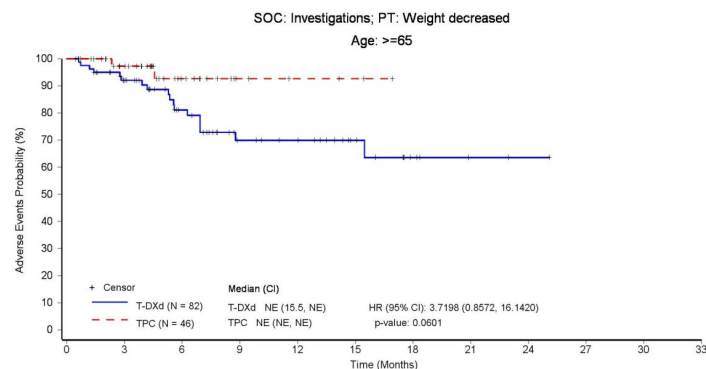
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 289)	289	231	168	118	74	52	33	17	6	2	0	0
TPC (N = 126)	126	70	27	11	5	3	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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 Data Intelligence – Evidence Generation  
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Patients still at risk:

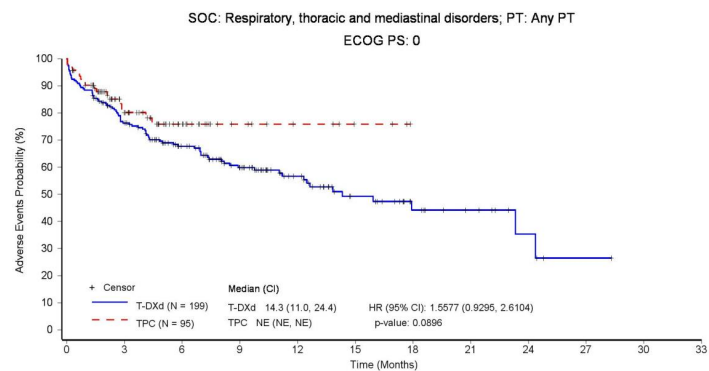
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 82)	82	60	40	23	20	12	5	2	1	0	0	0
TPC (N = 46)	46	33	14	5	3	2	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

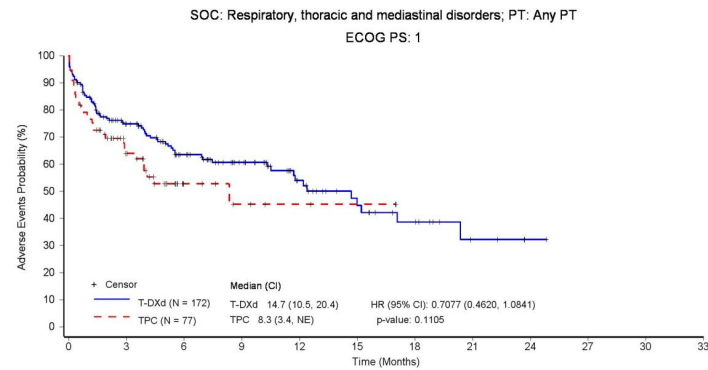
T-DXd (N = 199)	199	141	104	75	45	26	14	9	4	1	0	0
TPC (N = 95)	95	48	23	10	6	3	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

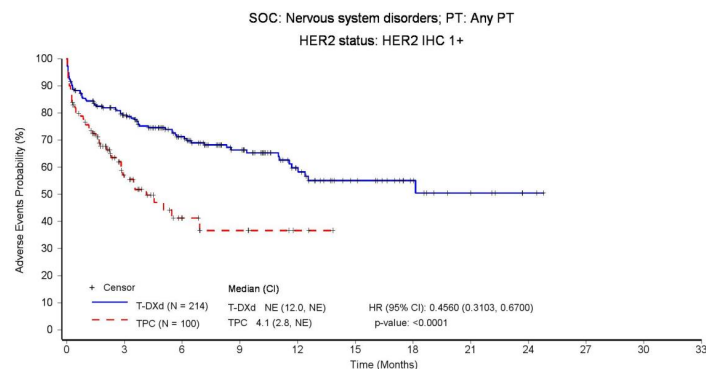
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 172)	172	109	72	50	28	17	11	4	1	0	0	0
TPC (N = 77)	77	33	10	5	3	2	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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Patients still at risk:

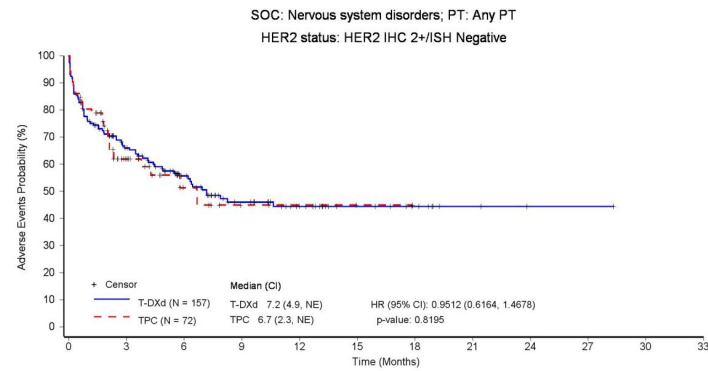
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 214)	214	142	99	69	39	23	13	6	2	0	0	0
TPC (N = 100)	100	33	11	6	2	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 157)	157	89	56	35	21	12	8	3	1	1	0	0
TPC (N = 72)	72	28	9	3	2	1	0	0	0	0	0	0

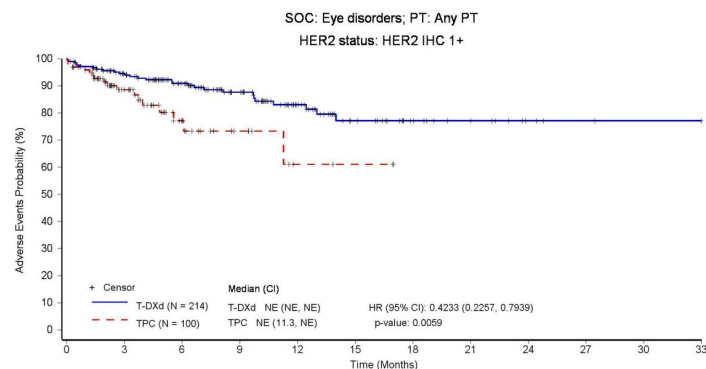
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

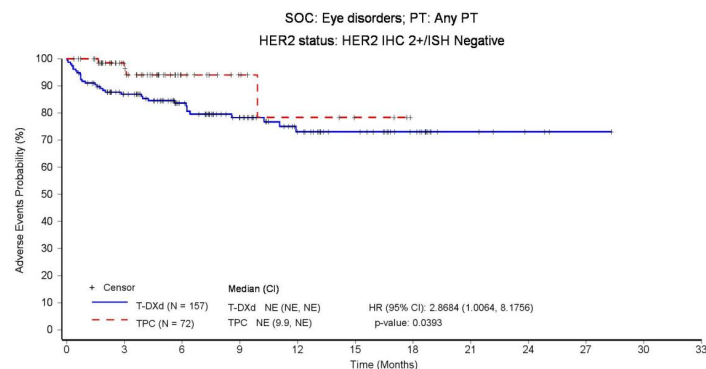
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 214)	214	168	127	90	53	28	16	9	4	2	1	0
TPC (N = 100)	100	53	22	9	3	2	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

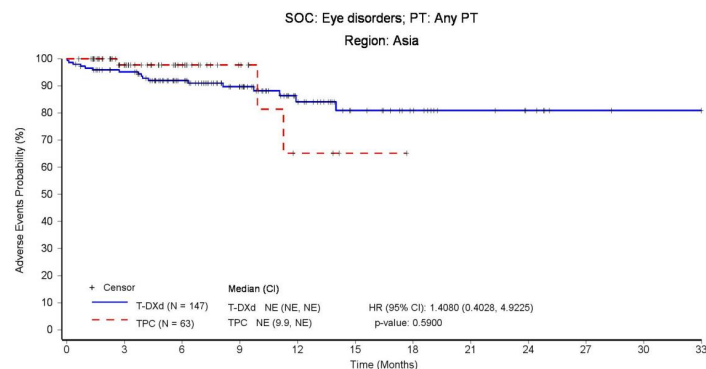
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 157)	157	117	84	59	36	26	16	6	3	1	0	0
TPC (N = 72)	72	45	16	8	5	3	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.4.7.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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Patients still at risk:

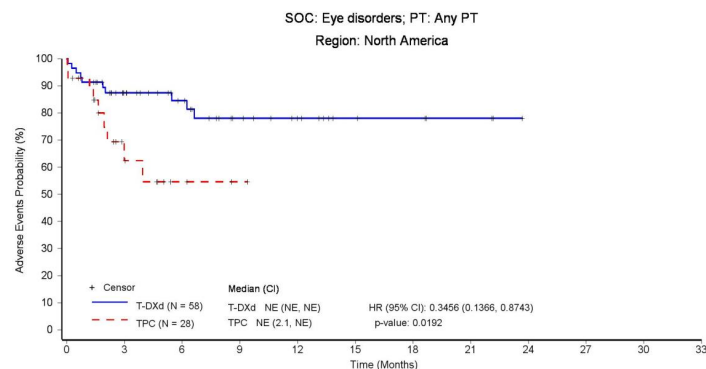
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 147)	147	127	93	68	37	22	15	9	6	2	1	0
TPC (N = 63)	63	39	20	9	3	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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Patients still at risk:

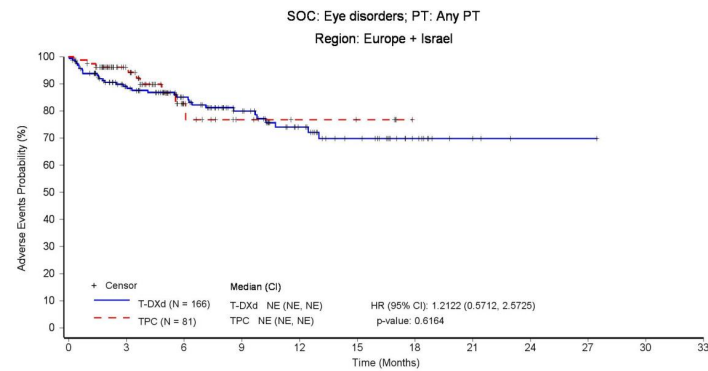
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 58)	58	38	28	18	12	6	5	3	0	0	0	0
TPC (N = 28)	28	9	3	1	0	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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Patients still at risk:

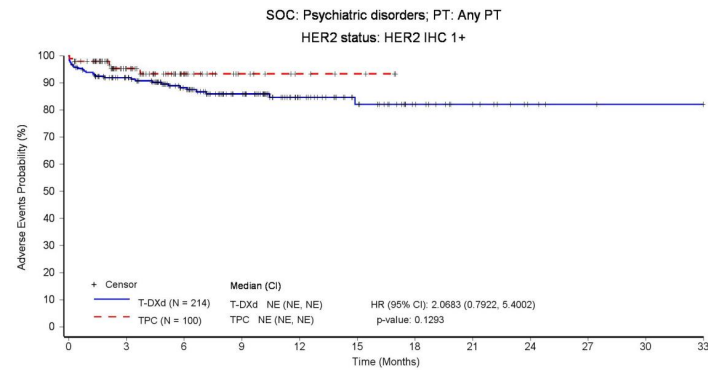
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 166)	166	120	90	63	40	26	12	3	1	1	0	0
TPC (N = 81)	81	50	15	7	5	4	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

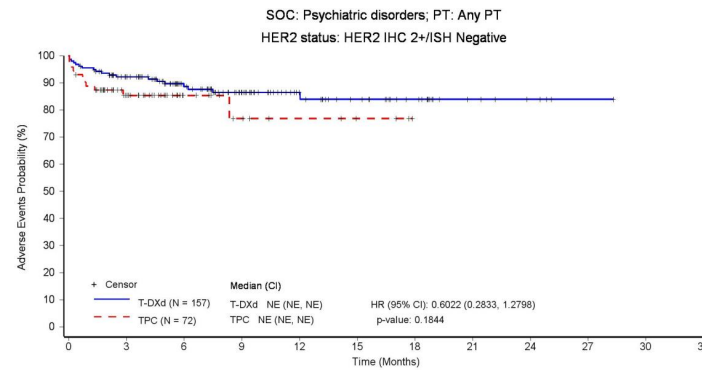
T-DXd (N = 214)	214	166	122	88	51	32	18	10	4	2	1	0
TPC (N = 100)	100	56	25	10	5	3	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

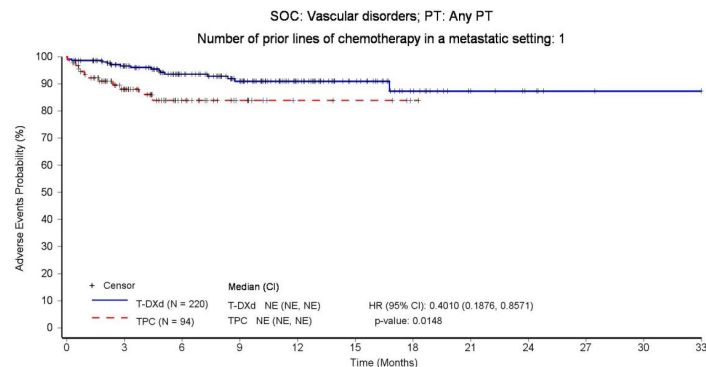
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 157)	157	126	87	59	35	26	17	7	4	1	0	0
TPC (N = 72)	72	40	14	8	5	3	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 220)	220	179	130	97	60	37	18	8	5	2	1	0
TPC (N = 94)	94	54	24	12	5	4	1	0	0	0	0	0

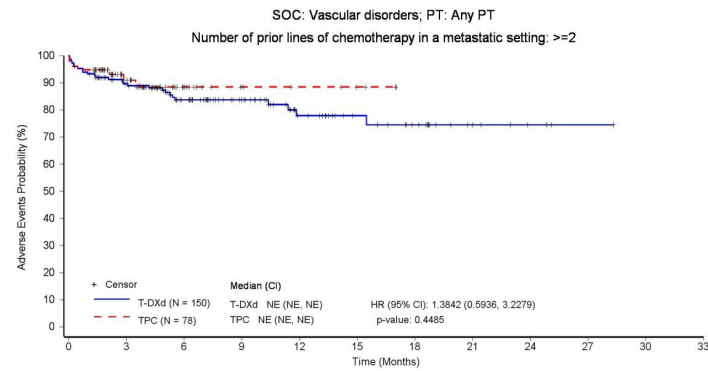
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf



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Patients still at risk:

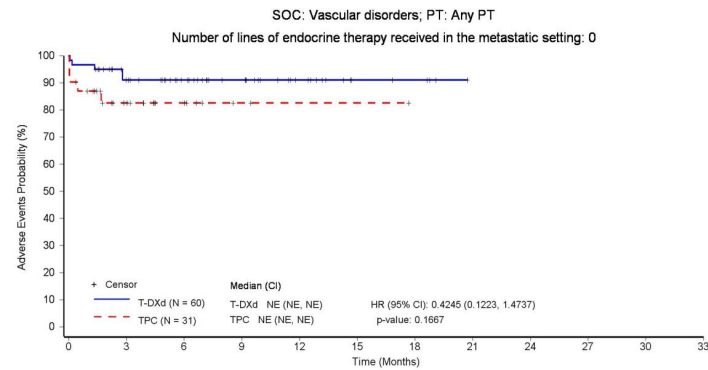
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 150)	150	118	84	58	35	23	16	6	3	1	0	0
TPC (N = 78)	78	42	16	7	5	3	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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Patients still at risk:

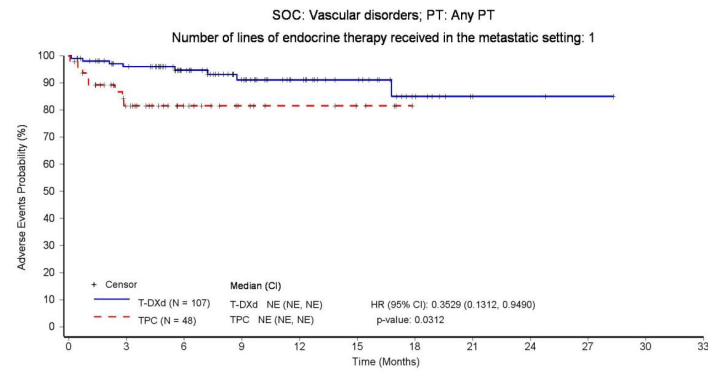
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 60)	60	46	32	23	13	5	4	0	0	0	0	0
TPC (N = 31)	31	14	7	2	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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Patients still at risk:

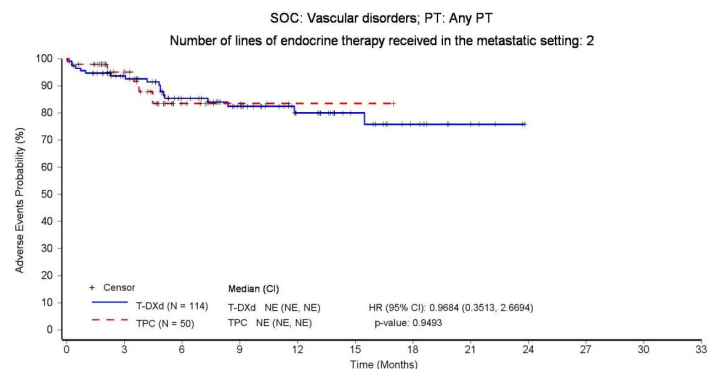
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 107)	107	89	66	45	30	21	9	2	2	1	0	0
TPC (N = 48)	48	30	16	9	6	4	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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Patients still at risk:

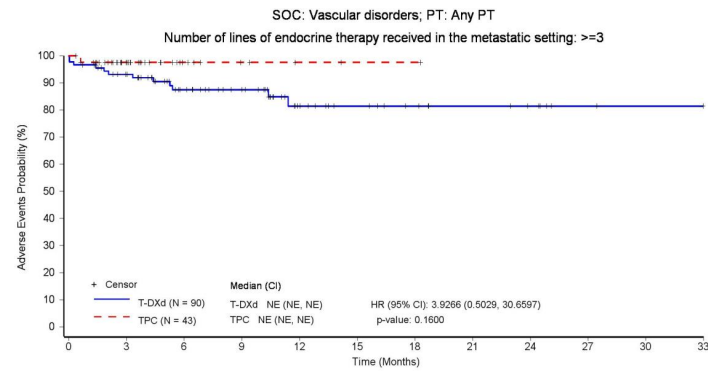
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 114)	114	87	64	48	31	19	10	4	0	0	0	0
TPC (N = 50)	50	29	9	4	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

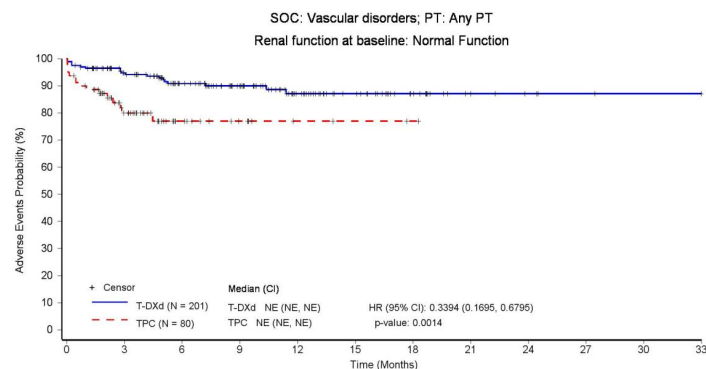
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 90)	90	76	53	39	21	15	11	8	6	2	1	0
TPC (N = 43)	43	23	8	4	2	1	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

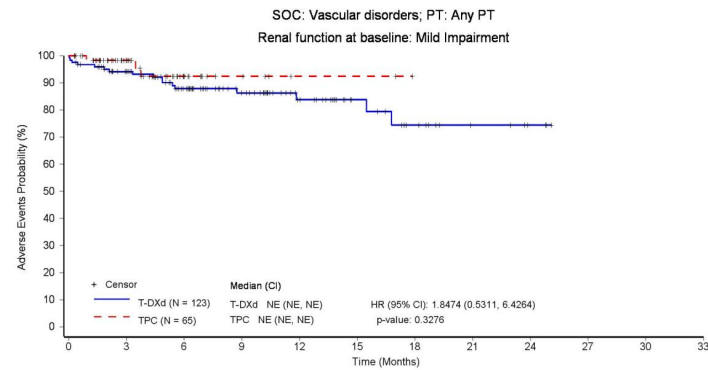
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 201)	201	163	114	85	50	33	18	6	4	2	1	0
TPC (N = 80)	80	39	16	8	3	2	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

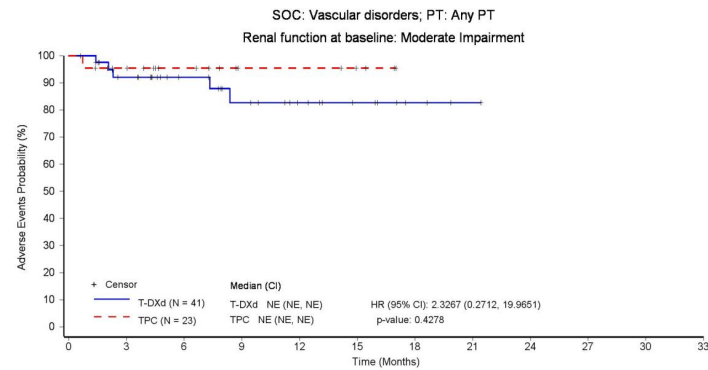
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 123)	123	100	75	52	33	19	12	6	3	0	0	0
TPC (N = 65)	65	38	14	6	2	2	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 41)	41	32	23	16	11	7	3	1	0	0	0	0
TPC (N = 23)	23	17	10	5	5	3	0	0	0	0	0	0

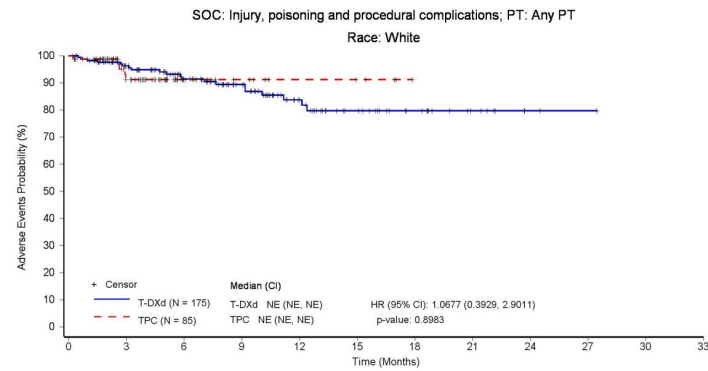
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

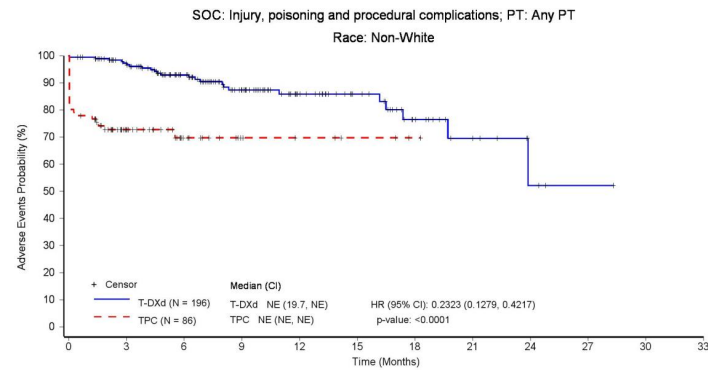
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 175)	175	137	99	73	42	28	16	8	2	1	0	0
TPC (N = 85)	85	46	18	9	5	4	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

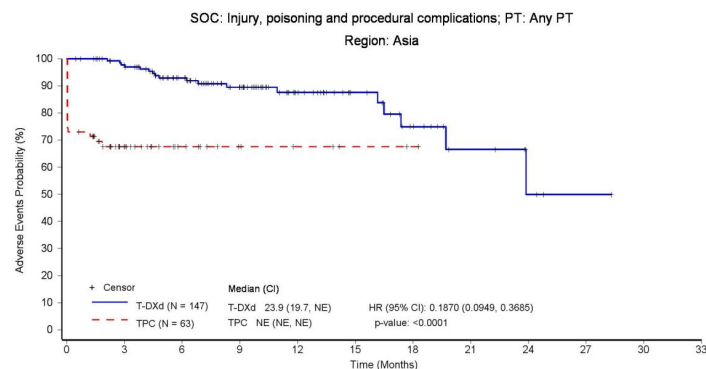
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 196)	196	167	119	80	47	33	18	8	3	1	0	0
TPC (N = 86)	86	39	16	7	5	3	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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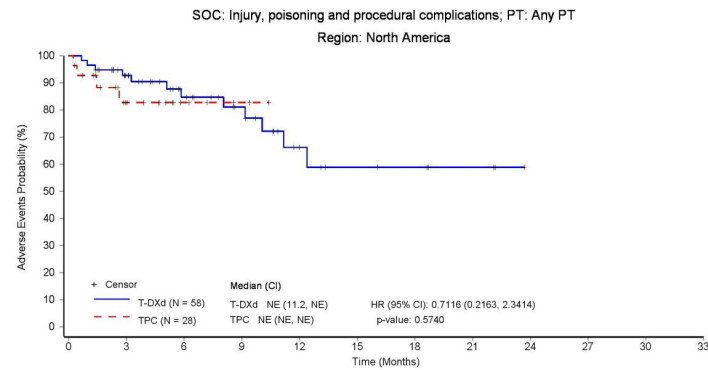
T-DXd (N = 147)	147	129	93	66	37	24	14	7	3	1	0	0
TPC (N = 63)	63	25	12	6	4	2	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.4.7.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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Patients still at risk:

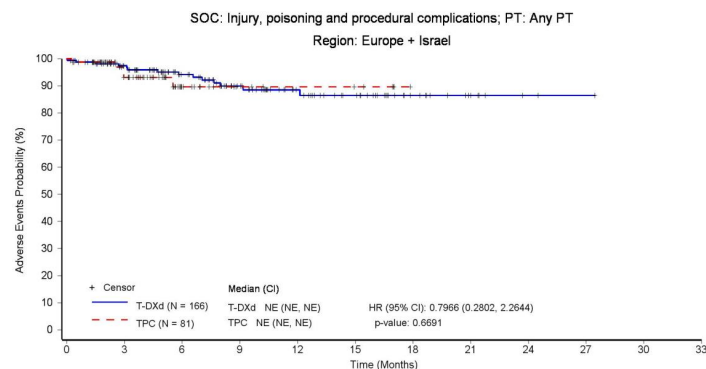
T-DXd (N = 58)	58	42	28	20	9	6	5	3	0	0	0	0
TPC (N = 28)	28	13	5	2	0	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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Patients still at risk:

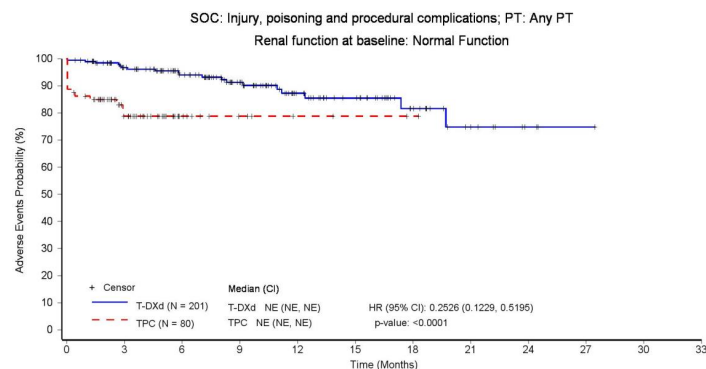
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 166)	166	133	97	67	43	31	15	6	2	1	0	0
TPC (N = 81)	81	48	17	8	6	5	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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Patients still at risk:

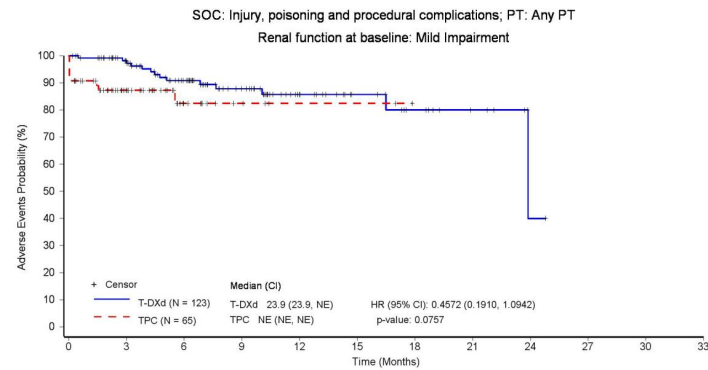
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 201)	201	167	121	87	51	37	19	8	3	1	0	0
TPC (N = 80)	80	36	12	6	3	2	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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Patients still at risk:

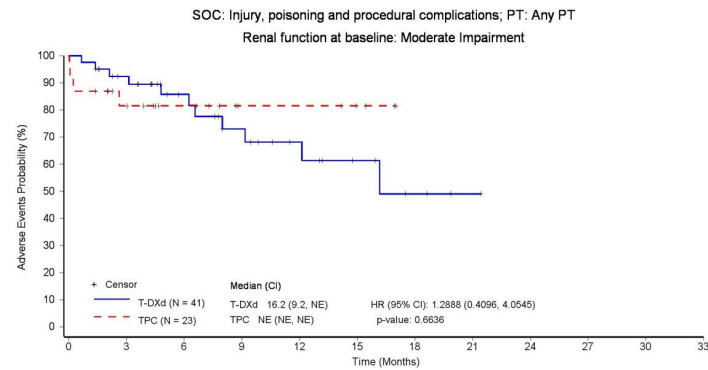
T-DXd (N = 123)	123	101	73	49	27	17	11	6	1	0	0	0
TPC (N = 65)	65	34	12	5	2	2	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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Patients still at risk:

T-DXd (N = 41)	41	32	21	15	10	6	3	1	0	0	0	0
TPC (N = 23)	23	15	10	5	5	3	0	0	0	0	0	0

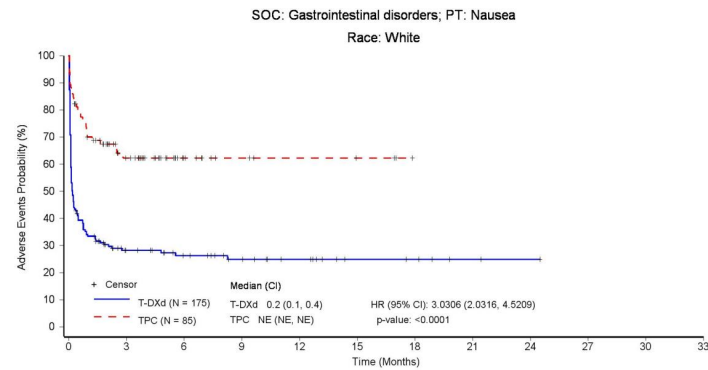
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

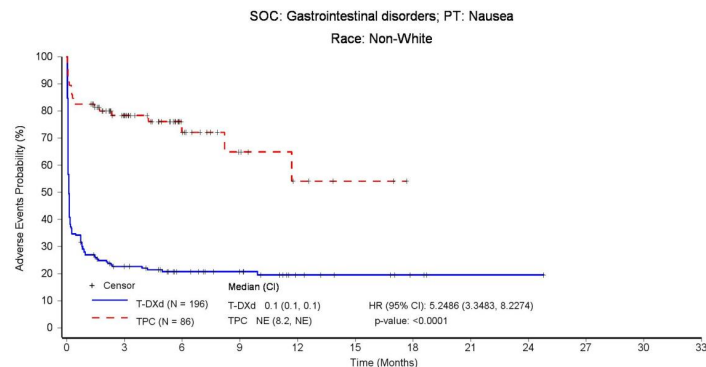
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 175)	175	34	25	17	12	6	5	2	1	0	0	0
TPC (N = 85)	85	34	12	6	4	3	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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Patients still at risk:

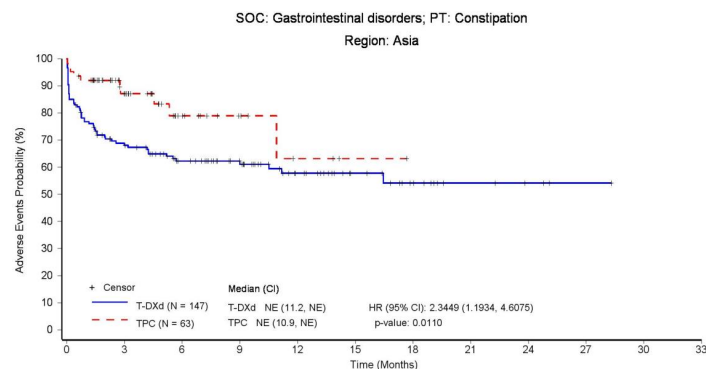
T-DXd (N = 196)	196	39	27	20	10	7	3	1	1	0	0	0
TPC (N = 86)	86	45	18	8	4	2	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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Patients still at risk:

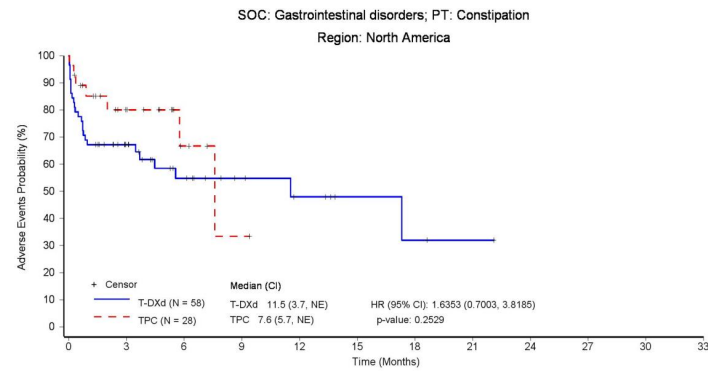
T-DXd (N = 147)	147	89	64	50	29	18	11	5	3	1	0	0
TPC (N = 63)	63	34	14	7	3	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

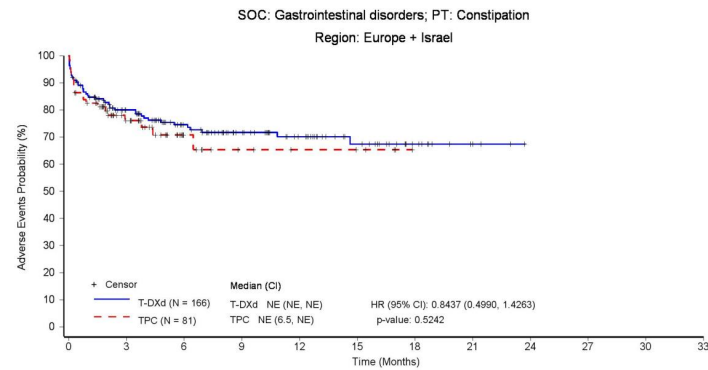
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 58)	58	27	15	9	6	3	2	1	0	0	0	0
TPC (N = 28)	28	13	4	1	0	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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Patients still at risk:

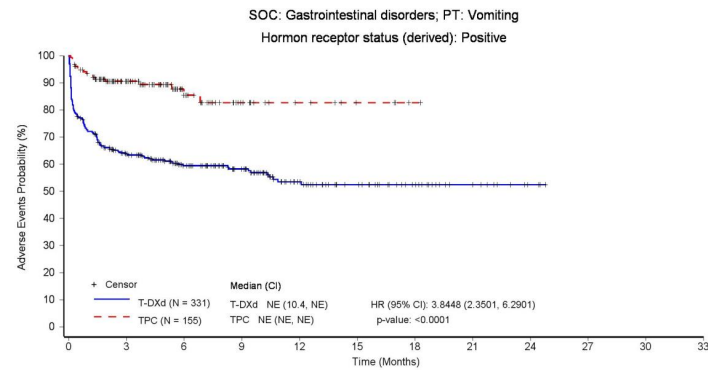
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 166)	166	109	80	57	39	25	12	3	0	0	0	0
TPC (N = 81)	81	38	13	7	5	4	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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Patients still at risk:

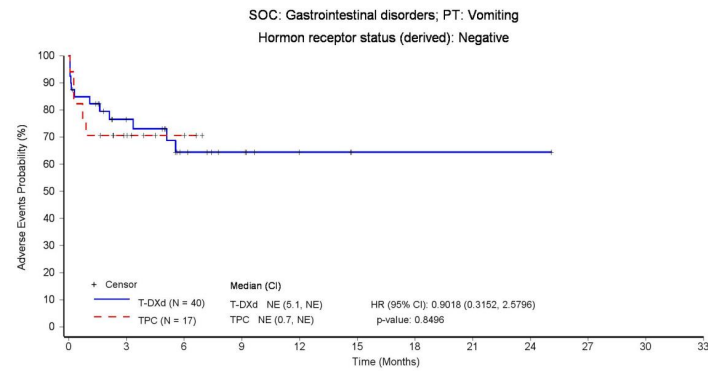
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 331)	331	183	131	92	51	35	22	10	3	0	0	0
TPC (N = 155)	155	90	36	16	8	4	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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Patients still at risk:

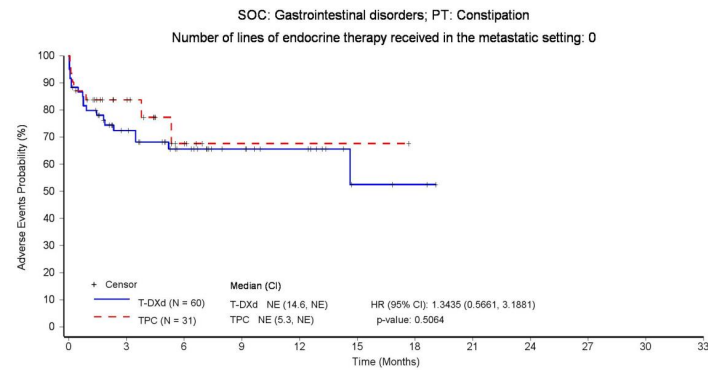
T-DXd (N = 40)	40	22	11	7	3	1	1	1	1	0	0	0
TPC (N = 17)	17	7	3	0	0	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 60)	60	35	23	15	11	3	2	0	0	0	0	0
TPC (N = 31)	31	15	5	1	1	1	0	0	0	0	0	0

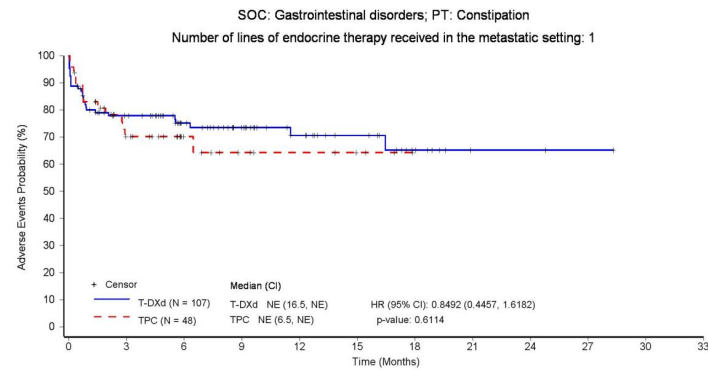
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

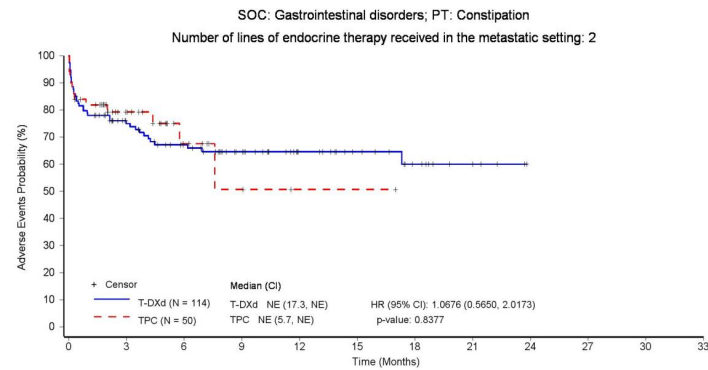
T-DXd (N = 107)	107	69	48	35	23	16	8	2	2	1	0	0
TPC (N = 48)	48	25	12	7	5	3	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

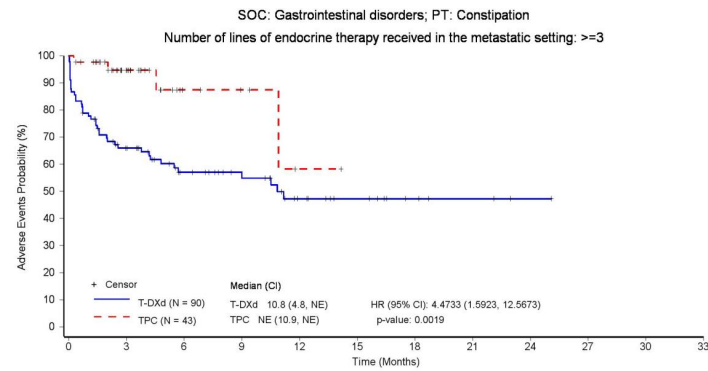
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 114)	114	69	54	40	25	17	10	4	0	0	0	0
TPC (N = 50)	50	23	8	3	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

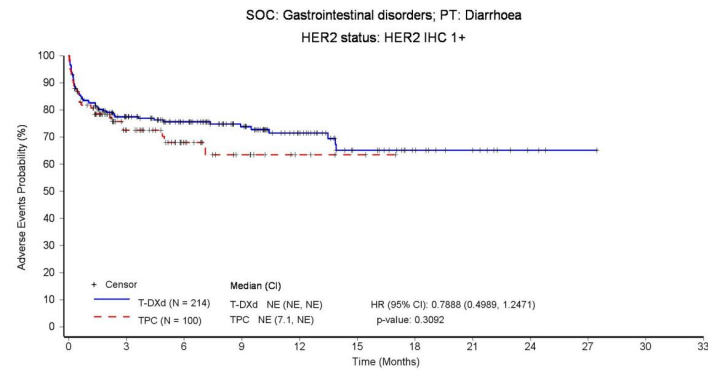
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 90)	90	52	34	26	15	10	5	3	1	0	0	0
TPC (N = 43)	43	22	6	4	1	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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Patients still at risk:

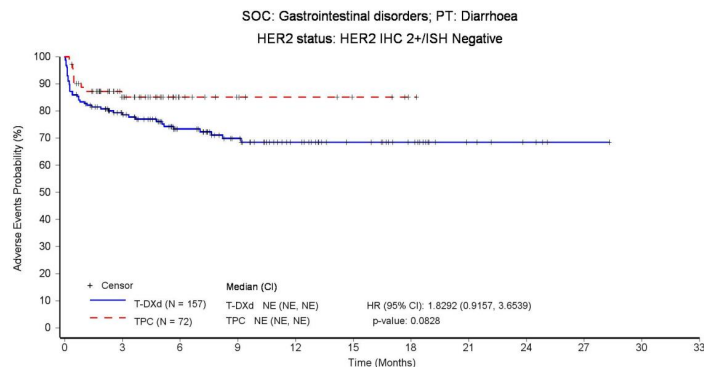
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 214)	214	137	104	76	46	26	16	9	3	1	0	0
TPC (N = 100)	100	43	21	10	4	2	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.4.7.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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Patients still at risk:

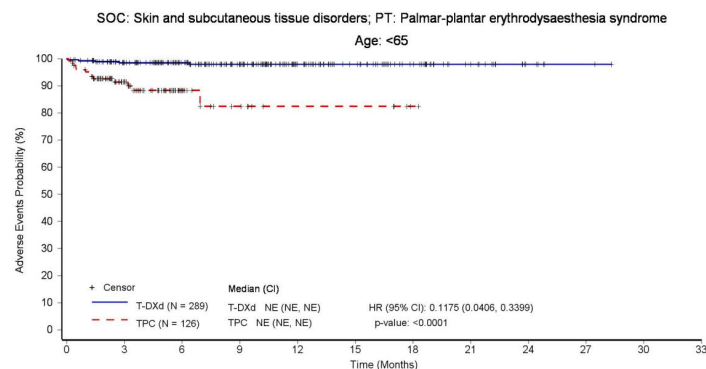
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 157)	157	103	71	52	33	23	16	7	4	1	0	0
TPC (N = 72)	72	39	13	8	6	4	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.4.7.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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Patients still at risk:

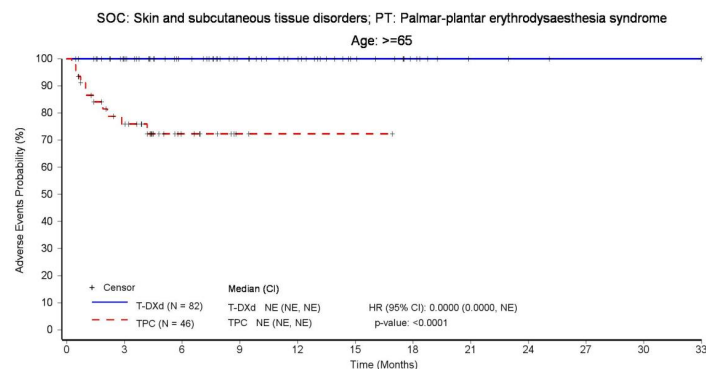
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 289)	289	245	186	137	83	57	36	17	6	2	0	0
TPC (N = 126)	126	65	22	10	5	5	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 D.E.F.4.7.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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Patients still at risk:

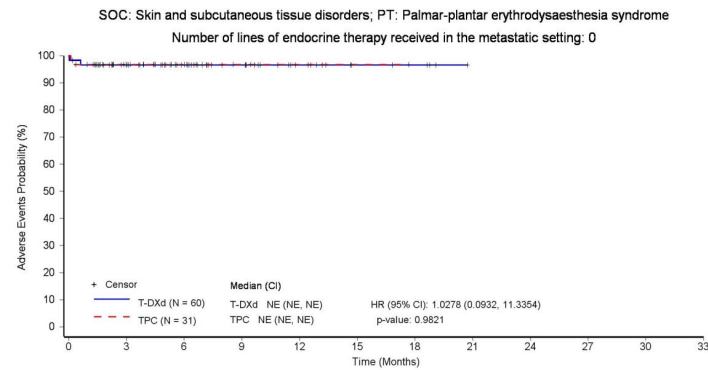
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 82)	82	65	49	35	27	16	8	3	2	1	1	0
TPC (N = 46)	46	27	9	2	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 60)	60	47	33	22	12	5	4	0	0	0	0	0
TPC (N = 31)	31	17	7	2	1	1	0	0	0	0	0	0

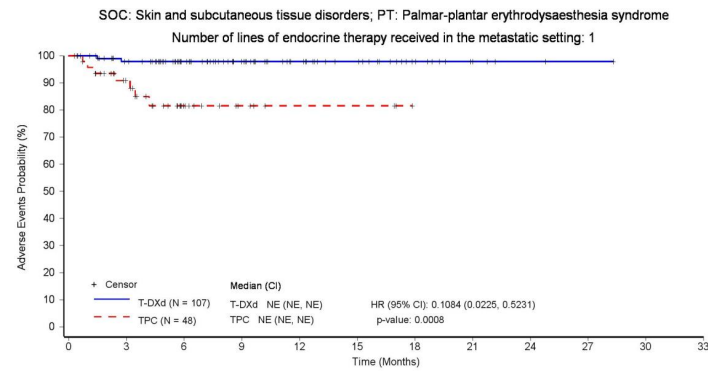
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf



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 DE.F.4.7.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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Patients still at risk:

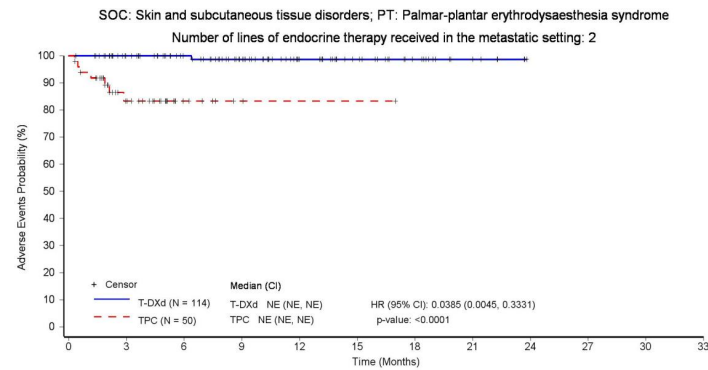
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 107)	107	89	65	45	31	22	11	4	2	1	0	0
TPC (N = 48)	48	32	13	6	3	3	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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 DE.F.4.7.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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Patients still at risk:

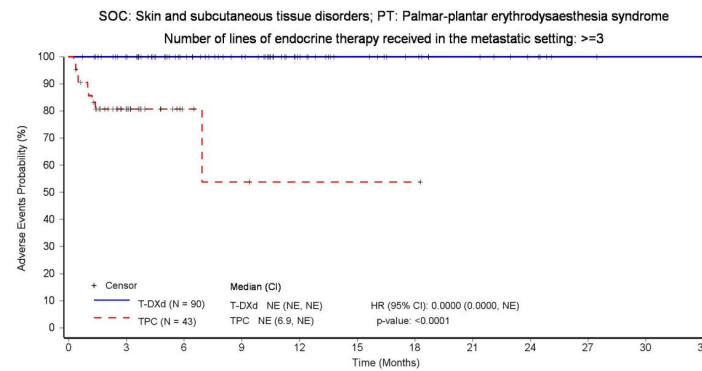
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 114)	114	93	77	60	39	26	15	6	0	0	0	0
TPC (N = 50)	50	25	7	2	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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Patients still at risk:

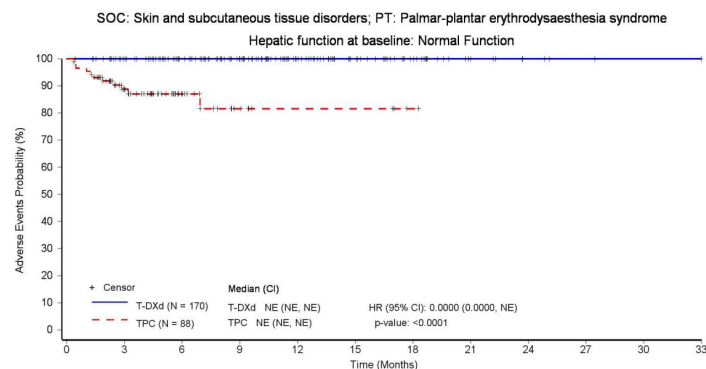
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 90)	90	81	60	45	28	20	14	10	6	2	1	0
TPC (N = 43)	43	18	4	2	1	1	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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Patients still at risk:

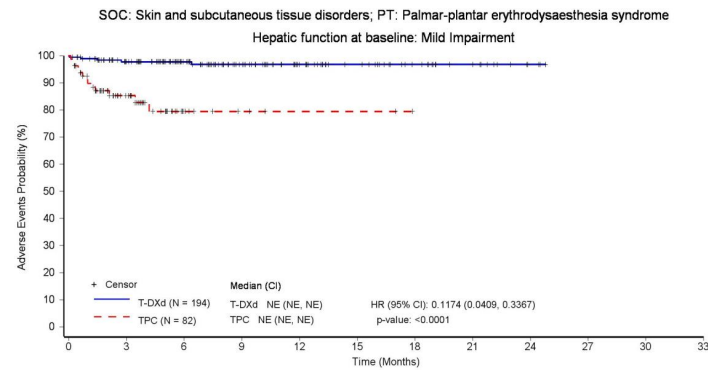
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 170)	170	155	126	99	62	40	22	8	4	2	1	0
TPC (N = 88)	88	54	21	8	4	4	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:16; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PER\_4\_SAS.rf

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 DE.F.4.7.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 10% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 194)	194	152	107	71	47	32	21	11	3	0	0	0
TPC (N = 82)	82	38	10	4	2	2	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.8.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	328 (88.4)	117 (68.0)	
Number of subjects censored, n (%)	43 (11.6)	55 (32.0)	
Median time to first event (months) [a]	0.1	0.7	
95% Confidence Interval	[0.1, 0.1]	[0.5, 1.4]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			2.0839
95% Confidence Interval			[1.6774, 2.5888]
p-value			<0.0001
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 13SEP2022 – 17:37; Program name: T4\_AESOCPT10PAT\_1\_SAS.sas; Output name: T4\_AESOCPT10PAT\_1\_SAS.rtf

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DE.T.4.8.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Nausea

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	282 (76.0)	52 (30.2)	
Number of subjects censored, n (%)	89 (24.0)	120 (69.8)	
Median time to first event (months) [a]	0.1	NE	
95% Confidence Interval	[0.1, 0.2]	[11.7, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			3.9712
95% Confidence Interval			[2.9469, 5.3516]
p-value			<0.0001
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:37; Program name: T4\_AESOCPT10PAT\_1\_SAS.sas; Output name: T4\_AESOCPT10PAT\_1\_SAS.rtf

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DE.T.4.8.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Vomiting

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	150 (40.4)	23 (13.4)	
Number of subjects censored, n (%)	221 (59.6)	149 (86.6)	
Median time to first event (months) [a] 95% Confidence Interval	NE [10.6, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			3.1400 [2.0200, 4.8808] <0.0001
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
Run date: 13SEP2022 – 17:37; Program name: T4\_AESOCPT10PAT\_1\_SAS.sas; Output name: T4\_AESOCPT10PAT\_1\_SAS.rtf



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DE.T.4.8.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Constipation

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	126 (34.0)	38 (22.1)	
Number of subjects censored, n (%)	245 (66.0)	134 (77.9)	
Median time to first event (months) [a] 95% Confidence Interval	NE [17.3, NE]	NE [10.9, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.3871 [0.9607, 2.0026] 0.0808
Stratified log-rank p-value [c]			0.0807

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:37; Program name: T4\_AESOCPT10PAT\_1\_SAS.sas; Output name: T4\_AESOCPT10PAT\_1\_SAS.rtf

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DE.T.4.8.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Diarrhoea

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	100 (27.0)	38 (22.1)	
Number of subjects censored, n (%)	271 (73.0)	134 (77.9)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.1163 [0.7644, 1.6304] 0.5690
Stratified log-rank p-value [c]			0.5727

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:37; Program name: T4\_AESOCPT10PAT\_1\_SAS.sas; Output name: T4\_AESOCPT10PAT\_1\_SAS.rtf

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DE.T.4.8.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Stomatitis

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	41 (11.1)	17 (9.9)	
Number of subjects censored, n (%)	330 (88.9)	155 (90.1)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.8472 [0.4777, 1.5027] 0.5707
Stratified log-rank p-value [c]			0.5718

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:37; Program name: T4\_AESOCPT10PAT\_1\_SAS.sas; Output name: T4\_AESOCPT10PAT\_1\_SAS.rtf

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DE.T.4.8.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Abdominal pain

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	35 (9.4)	8 (4.7)	
Number of subjects censored, n (%)	336 (90.6)	164 (95.3)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.5477 [0.7080, 3.3830] 0.2737
Stratified log-rank p-value [c]			0.2708

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.8.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Dyspepsia

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	34 (9.2)	11 (6.4)	
Number of subjects censored, n (%)	337 (90.8)	161 (93.6)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.1229 [0.5639, 2.2361] 0.7415
Stratified log-rank p-value [c]			0.7404

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Gastrointestinal disorders; PT: Abdominal pain upper

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	31 (8.4)	13 (7.6)	
Number of subjects censored, n (%)	340 (91.6)	159 (92.4)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.8762 [0.4529, 1.6954] 0.6948
Stratified log-rank p-value [c]			0.6913

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Gastrointestinal disorders; PT: Dry mouth

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	26 (7.0)	9 (5.2)	
Number of subjects censored, n (%)	345 (93.0)	163 (94.8)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.1311 [0.5259, 2.4327] 0.7526
Stratified log-rank p-value [c]			0.7524

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Gastrointestinal disorders; PT: Gastrooesophageal reflux disease

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	23 (6.2)	3 (1.7)	
Number of subjects censored, n (%)	348 (93.8)	169 (98.3)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			2.8883 [0.8594, 9.7078] 0.0864
Stratified log-rank p-value [c]			0.0728

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Gastrointestinal disorders; PT: Abdominal distension

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	20 (5.4)	5 (2.9)	
Number of subjects censored, n (%)	351 (94.6)	167 (97.1)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.7731 [0.6650, 4.7279] 0.2524
Stratified log-rank p-value [c]			0.2459

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Gastrointestinal disorders; PT: Gastritis

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	10 (2.7)	1 (0.6)	
Number of subjects censored, n (%)	361 (97.3)	171 (99.4)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			4.2570 [0.5437, 33.3298] 0.1677
Stratified log-rank p-value [c]			0.1329

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Investigations; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	251 (67.7)	114 (66.3)	
Number of subjects censored, n (%)	120 (32.3)	58 (33.7)	
Median time to first event (months) [a]	3.0	0.7	
95% Confidence Interval	[2.2, 4.1]	[0.5, 1.4]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.7105
95% Confidence Interval			[0.5659, 0.8920]
p-value			0.0032
Stratified log-rank p-value [c]			0.0030

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Investigations; PT: Aspartate aminotransferase increased

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	92 (24.8)	42 (24.4)	
Number of subjects censored, n (%)	279 (75.2)	130 (75.6)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [13.6, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.7891 [0.5422, 1.1485] 0.2161
Stratified log-rank p-value [c]			0.2124

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Investigations; PT: Neutrophil count decreased

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	81 (21.8)	62 (36.0)	
Number of subjects censored, n (%)	290 (78.2)	110 (64.0)	
Median time to first event (months) [a]	24.8	NE	
95% Confidence Interval	[24.8, NE]	[6.9, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.4034
95% Confidence Interval			[0.2871, 0.5669]
p-value			<0.0001
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Investigations; PT: White blood cell count decreased

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	78 (21.0)	49 (28.5)	
Number of subjects censored, n (%)	293 (79.0)	123 (71.5)	
Median time to first event (months) [a]	24.8	NE	
95% Confidence Interval	[24.8, NE]	[NE, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.5252
95% Confidence Interval			[0.3641, 0.7574]
p-value			0.0006
Stratified log-rank p-value [c]			0.0005

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Investigations; PT: Alanine aminotransferase increased

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	75 (20.2)	43 (25.0)	
Number of subjects censored, n (%)	296 (79.8)	129 (75.0)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [13.6, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.6585 [0.4493, 0.9650] 0.0321
Stratified log-rank p-value [c]			0.0315

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Investigations; PT: Platelet count decreased

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	73 (19.7)	12 (7.0)	
Number of subjects censored, n (%)	298 (80.3)	160 (93.0)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			2.3530 [1.2708, 4.3568] 0.0065
Stratified log-rank p-value [c]			0.0054

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: Weight decreased

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	60 (16.2)	14 (8.1)	
Number of subjects censored, n (%)	311 (83.8)	158 (91.9)	
Median time to first event (months) [a]	NE	NE	
95% Confidence Interval	[NE, NE]	[NE, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			1.3193
95% Confidence Interval			[0.7291, 2.3870]
p-value			0.3598
Stratified log-rank p-value [c]			0.3594

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.8.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Blood alkaline phosphatase increased

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	36 (9.7)	5 (2.9)	
Number of subjects censored, n (%)	335 (90.3)	167 (97.1)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			2.2581 [0.8758, 5.8225] 0.0919
Stratified log-rank p-value [c]			0.0834

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: Lymphocyte count decreased

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	29 (7.8)	12 (7.0)	
Number of subjects censored, n (%)	342 (92.2)	160 (93.0)	
Median time to first event (months) [a] 95% Confidence Interval	NE [24.8, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.8520 [0.4268, 1.7010] 0.6499
Stratified log-rank p-value [c]			0.6475

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: Blood bilirubin increased

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	26 (7.0)	7 (4.1)	
Number of subjects censored, n (%)	345 (93.0)	165 (95.9)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.0584 [0.4472, 2.5052] 0.8972
Stratified log-rank p-value [c]			0.8970

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: Gamma-glutamyltransferase increased

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	20 (5.4)	8 (4.7)	
Number of subjects censored, n (%)	351 (94.6)	164 (95.3)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.9113 [0.3959, 2.0978] 0.8271
Stratified log-rank p-value [c]			0.8257

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Investigations; PT: Blood lactate dehydrogenase increased

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	19 (5.1)	9 (5.2)	
Number of subjects censored, n (%)	352 (94.9)	163 (94.8)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.7870 [0.3484, 1.7779] 0.5646
Stratified log-rank p-value [c]			0.5641

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Investigations; PT: Ejection fraction decreased

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	16 (4.3)	0	
Number of subjects censored, n (%)	355 (95.7)	172 (100)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			NE [0.0000, NE] 0.9932
Stratified log-rank p-value [c]			0.0481

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Investigations; PT: Blood creatinine increased

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	14 (3.8)	7 (4.1)	
Number of subjects censored, n (%)	357 (96.2)	165 (95.9)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [14.4, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.6517 [0.2560, 1.6589] 0.3691
Stratified log-rank p-value [c]			0.3660

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Investigations; PT: Electrocardiogram QT prolonged

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	11 (3.0)	4 (2.3)	
Number of subjects censored, n (%)	360 (97.0)	168 (97.7)	
Median time to first event (months) [a]	NE	NE	
95% Confidence Interval	[NE, NE]	[NE, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.6550
95% Confidence Interval			[0.1970, 2.1773]
p-value			0.4900
Stratified log-rank p-value [c]			0.4876

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.8.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: General disorders and administration site conditions; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	248 (66.8)	102 (59.3)	
Number of subjects censored, n (%)	123 (33.2)	70 (40.7)	
Median time to first event (months) [a]	2.1	1.4	
95% Confidence Interval	[1.3, 3.4]	[0.7, 3.3]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.9693
95% Confidence Interval			[0.7662, 1.2262]
p-value			0.7947
Stratified log-rank p-value [c]			0.7786

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: General disorders and administration site conditions; PT: Fatigue

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	110 (29.6)	50 (29.1)	
Number of subjects censored, n (%)	261 (70.4)	122 (70.9)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.8950 [0.6374, 1.2568] 0.5220
Stratified log-rank p-value [c]			0.5086

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: General disorders and administration site conditions; PT: Asthenia

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	70 (18.9)	25 (14.5)	
Number of subjects censored, n (%)	301 (81.1)	147 (85.5)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.1539 [0.7263, 1.8333] 0.5445
Stratified log-rank p-value [c]			0.5569

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: General disorders and administration site conditions; PT: Pyrexia

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	46 (12.4)	22 (12.8)	
Number of subjects censored, n (%)	325 (87.6)	150 (87.2)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.5691 [0.3341, 0.9694] 0.0381
Stratified log-rank p-value [c]			0.0354

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: General disorders and administration site conditions; PT: Malaise

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	33 (8.9)	11 (6.4)	
Number of subjects censored, n (%)	338 (91.1)	161 (93.6)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.2022 [0.6029, 2.3973] 0.6010
Stratified log-rank p-value [c]			0.5994

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: General disorders and administration site conditions; PT: Oedema peripheral

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	25 (6.7)	10 (5.8)	
Number of subjects censored, n (%)	346 (93.3)	162 (94.2)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.7087 [0.3303, 1.5205] 0.3766
Stratified log-rank p-value [c]			0.3746

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: General disorders and administration site conditions; PT: Chills

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	13 (3.5)	3 (1.7)	
Number of subjects censored, n (%)	358 (96.5)	169 (98.3)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.5562 [0.4355, 5.5603] 0.4961
Stratified log-rank p-value [c]			0.4940

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: General disorders and administration site conditions; PT: Mucosal inflammation

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	11 (3.0)	6 (3.5)	
Number of subjects censored, n (%)	360 (97.0)	166 (96.5)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.5894 [0.2104, 1.6511] 0.3145
Stratified log-rank p-value [c]			0.3100

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: General disorders and administration site conditions; PT: Non-cardiac chest pain

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	10 (2.7)	6 (3.5)	
Number of subjects censored, n (%)	361 (97.3)	166 (96.5)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.5106 [0.1735, 1.5025] 0.2222
Stratified log-rank p-value [c]			0.2144

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Skin and subcutaneous tissue disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	195 (52.6)	92 (53.5)	
Number of subjects censored, n (%)	176 (47.4)	80 (46.5)	
Median time to first event (months) [a]	5.7	2.6	
95% Confidence Interval	[3.5, 8.2]	[1.1, 4.2]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.7094
95% Confidence Interval			[0.5504, 0.9145]
p-value			0.0081
Stratified log-rank p-value [c]			0.0076

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	147 (39.6)	57 (33.1)	
Number of subjects censored, n (%)	224 (60.4)	115 (66.9)	
Median time to first event (months) [a] 95% Confidence Interval	NE [16.0, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.0193 [0.7486, 1.3879] 0.9034
Stratified log-rank p-value [c]			0.9122

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Skin and subcutaneous tissue disorders; PT: Rash

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	24 (6.5)	9 (5.2)	
Number of subjects censored, n (%)	347 (93.5)	163 (94.8)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.8167 [0.3699, 1.8031] 0.6163
Stratified log-rank p-value [c]			0.6158

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Skin and subcutaneous tissue disorders; PT: Dry skin

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	16 (4.3)	4 (2.3)	
Number of subjects censored, n (%)	355 (95.7)	168 (97.7)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.3983 [0.4538, 4.3088] 0.5593
Stratified log-rank p-value [c]			0.5584

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Skin and subcutaneous tissue disorders; PT: Pruritus

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	12 (3.2)	7 (4.1)	
Number of subjects censored, n (%)	359 (96.8)	165 (95.9)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.5314 [0.1994, 1.4157] 0.2060
Stratified log-rank p-value [c]			0.1991

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Skin and subcutaneous tissue disorders; PT: Rash maculo-papular

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	10 (2.7)	4 (2.3)	
Number of subjects censored, n (%)	361 (97.3)	168 (97.7)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.6375 [0.1837, 2.2131] 0.4784
Stratified log-rank p-value [c]			0.4752

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysesthesia syndrome

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	5 (1.3)	24 (14.0)	
Number of subjects censored, n (%)	366 (98.7)	148 (86.0)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.0690 [0.0258, 0.1848] <0.0001
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Metabolism and nutrition disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	188 (50.7)	63 (36.6)	
Number of subjects censored, n (%)	183 (49.3)	109 (63.4)	
Median time to first event (months) [a]	7.2	NE	
95% Confidence Interval	[4.8, 11.8]	[6.5, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			1.3127
95% Confidence Interval			[0.9829, 1.7531]
p-value			0.0653
Stratified log-rank p-value [c]			0.0684

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	118 (31.8)	33 (19.2)	
Number of subjects censored, n (%)	253 (68.2)	139 (80.8)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.6305 [1.1047, 2.4067] 0.0139
Stratified log-rank p-value [c]			0.0135

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	39 (10.5)	12 (7.0)	
Number of subjects censored, n (%)	332 (89.5)	160 (93.0)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.1483 [0.5950, 2.2163] 0.6801
Stratified log-rank p-value [c]			0.6822

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.8.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Metabolism and nutrition disorders; PT: Hypoalbuminaemia

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	32 (8.6)	8 (4.7)	
Number of subjects censored, n (%)	339 (91.4)	164 (95.3)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.2502 [0.5657, 2.7628] 0.5810
Stratified log-rank p-value [c]			0.5814

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Metabolism and nutrition disorders; PT: Hypocalcaemia

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	19 (5.1)	5 (2.9)	
Number of subjects censored, n (%)	352 (94.9)	167 (97.1)	
Median time to first event (months) [a]	NE	NE	
95% Confidence Interval	[NE, NE]	[NE, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			1.3122
95% Confidence Interval			[0.4778, 3.6037]
p-value			0.5981
Stratified log-rank p-value [c]			0.5957

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Metabolism and nutrition disorders; PT: Hypercalcaemia

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	12 (3.2)	1 (0.6)	
Number of subjects censored, n (%)	359 (96.8)	171 (99.4)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			3.4370 [0.4353, 27.1382] 0.2416
Stratified log-rank p-value [c]			0.2132

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.8.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Metabolism and nutrition disorders; PT: Hyponatraemia

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	12 (3.2)	5 (2.9)	
Number of subjects censored, n (%)	359 (96.8)	167 (97.1)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.9243 [0.3202, 2.6687] 0.8844
Stratified log-rank p-value [c]			0.8868

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Metabolism and nutrition disorders; PT: Hypomagnesaemia

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	10 (2.7)	6 (3.5)	
Number of subjects censored, n (%)	361 (97.3)	166 (96.5)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.4884 [0.1703, 1.4011] 0.1826
Stratified log-rank p-value [c]			0.1741

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Blood and lymphatic system disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	179 (48.2)	74 (43.0)	
Number of subjects censored, n (%)	192 (51.8)	98 (57.0)	
Median time to first event (months) [a]	9.0	7.0	
95% Confidence Interval	[7.2, 12.0]	[4.1, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.7908
95% Confidence Interval			[0.5987, 1.0445]
p-value			0.0983
Stratified log-rank p-value [c]			0.0979

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Blood and lymphatic system disorders; PT: Anaemia

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	139 (37.5)	45 (26.2)	
Number of subjects censored, n (%)	232 (62.5)	127 (73.8)	
Median time to first event (months) [a]	24.8	NE	
95% Confidence Interval	[11.7, NE]	[15.4, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			1.0799
95% Confidence Interval			[0.7653, 1.5239]
p-value			0.6616
Stratified log-rank p-value [c]			0.6712

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Blood and lymphatic system disorders; PT: Neutropenia

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	49 (13.2)	31 (18.0)	
Number of subjects censored, n (%)	322 (86.8)	141 (82.0)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.5584 [0.3523, 0.8850] 0.0131
Stratified log-rank p-value [c]			0.0122

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	23 (6.2)	4 (2.3)	
Number of subjects censored, n (%)	348 (93.8)	168 (97.7)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [16.1, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.7923 [0.6082, 5.2815] 0.2900
Stratified log-rank p-value [c]			0.2839

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Blood and lymphatic system disorders; PT: Leukopenia

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	13 (3.5)	7 (4.1)	
Number of subjects censored, n (%)	358 (96.5)	165 (95.9)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.7318 [0.2891, 1.8520] 0.5098
Stratified log-rank p-value [c]			0.5082

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	155 (41.8)	50 (29.1)	
Number of subjects censored, n (%)	216 (58.2)	122 (70.9)	
Median time to first event (months) [a]	14.3	NE	
95% Confidence Interval	[11.8, 17.9]	[NE, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			1.0256
95% Confidence Interval			[0.7394, 1.4227]
p-value			0.8795
Stratified log-rank p-value [c]			0.8703

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	39 (10.5)	2 (1.2)	
Number of subjects censored, n (%)	332 (89.5)	170 (98.8)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			5.0895 [1.2150, 21.3202] 0.0260
Stratified log-rank p-value [c]			0.0134

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	38 (10.2)	16 (9.3)	
Number of subjects censored, n (%)	333 (89.8)	156 (90.7)	
Median time to first event (months) [a] 95% Confidence Interval	NE [24.4, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.8887 [0.4892, 1.6146] 0.6986
Stratified log-rank p-value [c]			0.6973

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.8.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Respiratory, thoracic and mediastinal disorders; PT: Cough

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	36 (9.7)	14 (8.1)	
Number of subjects censored, n (%)	335 (90.3)	158 (91.9)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.9022 [0.4796, 1.6972] 0.7496
Stratified log-rank p-value [c]			0.7518

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.8.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	28 (7.5)	0	
Number of subjects censored, n (%)	343 (92.5)	172 (100)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			NE [0.0000, NE] 0.9903
Stratified log-rank p-value [c]			0.0041

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.8.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	23 (6.2)	1 (0.6)	
Number of subjects censored, n (%)	348 (93.8)	171 (99.4)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			5.9222 [0.7882, 44.4963] 0.0839
Stratified log-rank p-value [c]			0.0498

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.8.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Respiratory, thoracic and mediastinal disorders; PT: Rhinorrhoea

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	14 (3.8)	3 (1.7)	
Number of subjects censored, n (%)	357 (96.2)	169 (98.3)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.5166 [0.4232, 5.4354] 0.5225
Stratified log-rank p-value [c]			0.5192

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.8.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Nervous system disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	146 (39.4)	75 (43.6)	
Number of subjects censored, n (%)	225 (60.6)	97 (56.4)	
Median time to first event (months) [a]	18.1	5.0	
95% Confidence Interval	[11.0, NE]	[3.0, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.6166
95% Confidence Interval			[0.4617, 0.8235]
p-value			0.0011
Stratified log-rank p-value [c]			0.0009

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Nervous system disorders; PT: Headache

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	54 (14.6)	11 (6.4)	
Number of subjects censored, n (%)	317 (85.4)	161 (93.6)	
Median time to first event (months) [a]	NE	NE	
95% Confidence Interval	[NE, NE]	[NE, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			1.8056
95% Confidence Interval			[0.9369, 3.4797]
p-value			0.0775
Stratified log-rank p-value [c]			0.0731

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.8.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Nervous system disorders; PT: Dysgeusia

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	37 (10.0)	16 (9.3)	
Number of subjects censored, n (%)	334 (90.0)	156 (90.7)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.8375 [0.4610, 1.5215] 0.5605
Stratified log-rank p-value [c]			0.5577

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Nervous system disorders; PT: Dizziness

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	32 (8.6)	9 (5.2)	
Number of subjects censored, n (%)	339 (91.4)	163 (94.8)	
Median time to first event (months) [a]	NE	NE	
95% Confidence Interval	[NE, NE]	[NE, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			1.2327
95% Confidence Interval			[0.5804, 2.6180]
p-value			0.5862
Stratified log-rank p-value [c]			0.5855

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.8.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	18 (4.9)	19 (11.0)	
Number of subjects censored, n (%)	353 (95.1)	153 (89.0)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.3367 [0.1748, 0.6487] 0.0011
Stratified log-rank p-value [c]			0.0007

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.8.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Nervous system disorders; PT: Neuropathy peripheral

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	13 (3.5)	16 (9.3)	
Number of subjects censored, n (%)	358 (96.5)	156 (90.7)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.2305 [0.1084, 0.4899] 0.0001
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.8.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	136 (36.7)	56 (32.6)	
Number of subjects censored, n (%)	235 (63.3)	116 (67.4)	
Median time to first event (months) [a]	16.5	11.0	
95% Confidence Interval	[12.1, NE]	[6.1, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.7321
95% Confidence Interval			[0.5301, 1.0109]
p-value			0.0582
Stratified log-rank p-value [c]			0.0574

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	43 (11.6)	20 (11.6)	
Number of subjects censored, n (%)	328 (88.4)	152 (88.4)	
Median time to first event (months) [a] 95% Confidence Interval	NE [22.7, NE]	NE [11.5, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.5833 [0.3352, 1.0152] 0.0566
Stratified log-rank p-value [c]			0.0539

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Musculoskeletal and connective tissue disorders; PT: Back pain

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	34 (9.2)	10 (5.8)	
Number of subjects censored, n (%)	337 (90.8)	162 (94.2)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.1263 [0.5492, 2.3101] 0.7455
Stratified log-rank p-value [c]			0.7465

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	29 (7.8)	5 (2.9)	
Number of subjects censored, n (%)	342 (92.2)	167 (97.1)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.7284 [0.6553, 4.5589] 0.2689
Stratified log-rank p-value [c]			0.2631

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.8.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	22 (5.9)	16 (9.3)	
Number of subjects censored, n (%)	349 (94.1)	156 (90.7)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.4347 [0.2229, 0.8477] 0.0145
Stratified log-rank p-value [c]			0.0121

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Musculoskeletal and connective tissue disorders; PT: Muscle spasms

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	17 (4.6)	3 (1.7)	
Number of subjects censored, n (%)	354 (95.4)	169 (98.3)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.4404 [0.4087, 5.0767] 0.5702
Stratified log-rank p-value [c]			0.5679

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Musculoskeletal and connective tissue disorders; PT: Bone pain

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	14 (3.8)	8 (4.7)	
Number of subjects censored, n (%)	357 (96.2)	164 (95.3)	
Median time to first event (months) [a]	NE	NE	
95% Confidence Interval	[NE, NE]	[NE, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.6163
95% Confidence Interval			[0.2539, 1.4962]
p-value			0.2848
Stratified log-rank p-value [c]			0.2831

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Infections and infestations; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	127 (34.2)	36 (20.9)	
Number of subjects censored, n (%)	244 (65.8)	136 (79.1)	
Median time to first event (months) [a]	18.0	NE	
95% Confidence Interval	[12.4, NE]	[NE, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			1.1578
95% Confidence Interval			[0.7921, 1.6924]
p-value			0.4493
Stratified log-rank p-value [c]			0.4512

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Infections and infestations; PT: Urinary tract infection

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	29 (7.8)	6 (3.5)	
Number of subjects censored, n (%)	342 (92.2)	166 (96.5)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.5370 [0.6249, 3.7807] 0.3493
Stratified log-rank p-value [c]			0.3458

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Infections and infestations; PT: Upper respiratory tract infection

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	16 (4.3)	1 (0.6)	
Number of subjects censored, n (%)	355 (95.7)	171 (99.4)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			5.1619 [0.6742, 39.5206] 0.1140
Stratified log-rank p-value [c]			0.0783

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Infections and infestations; PT: Pneumonia

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	15 (4.0)	3 (1.7)	
Number of subjects censored, n (%)	356 (96.0)	169 (98.3)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.5060 [0.4250, 5.3367] 0.5259
Stratified log-rank p-value [c]			0.5231

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Infections and infestations; PT: Nasopharyngitis

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	14 (3.8)	2 (1.2)	
Number of subjects censored, n (%)	357 (96.2)	170 (98.8)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.9929 [0.4418, 8.9897] 0.3696
Stratified log-rank p-value [c]			0.3605

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Eye disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	60 (16.2)	21 (12.2)	
Number of subjects censored, n (%)	311 (83.8)	151 (87.8)	
Median time to first event (months) [a]	NE	NE	
95% Confidence Interval	[NE, NE]	[11.3, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.8508
95% Confidence Interval			[0.5080, 1.4249]
p-value			0.5390
Stratified log-rank p-value [c]			0.5367

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Eye disorders; PT: Vision blurred

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	13 (3.5)	5 (2.9)	
Number of subjects censored, n (%)	358 (96.5)	167 (97.1)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.0398 [0.3656, 2.9571] 0.9416
Stratified log-rank p-value [c]			0.9411

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Eye disorders; PT: Dry eye

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	10 (2.7)	4 (2.3)	
Number of subjects censored, n (%)	361 (97.3)	168 (97.7)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.7375 [0.2179, 2.4964] 0.6246
Stratified log-rank p-value [c]			0.6235

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Psychiatric disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	47 (12.7)	16 (9.3)	
Number of subjects censored, n (%)	324 (87.3)	156 (90.7)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.0497 [0.5897, 1.8686] 0.8690
Stratified log-rank p-value [c]			0.8662

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Psychiatric disorders; PT: Insomnia

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	24 (6.5)	9 (5.2)	
Number of subjects censored, n (%)	347 (93.5)	163 (94.8)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.9779 [0.4482, 2.1340] 0.9553
Stratified log-rank p-value [c]			0.9559

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.8.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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SOC: Psychiatric disorders; PT: Anxiety

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	12 (3.2)	5 (2.9)	
Number of subjects censored, n (%)	359 (96.8)	167 (97.1)	
Median time to first event (months) [a]	NE	NE	
95% Confidence Interval	[NE, NE]	[NE, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.7994
95% Confidence Interval			[0.2783, 2.2963]
p-value			0.6775
Stratified log-rank p-value [c]			0.6769

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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DE.T.4.8.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Injury, poisoning and procedural complications; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	44 (11.9)	29 (16.9)	
Number of subjects censored, n (%)	327 (88.1)	143 (83.1)	
Median time to first event (months) [a] 95% Confidence Interval	NE [23.9, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.3769 [0.2293, 0.6196] 0.0001
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Injury, poisoning and procedural complications; PT: Fall

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	13 (3.5)	2 (1.2)	
Number of subjects censored, n (%)	358 (96.5)	170 (98.8)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.5956 [0.3517, 7.2387] 0.5448
Stratified log-rank p-value [c]			0.5413

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.8.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Injury, poisoning and procedural complications; PT: Medication error

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	0	11 (6.4)	
Number of subjects censored, n (%)	371 (100)	161 (93.6)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.0000 [0.0000, NE] 0.9927
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Injury, poisoning and procedural complications; PT: Contusion

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	10 (2.7)	1 (0.6)	
Number of subjects censored, n (%)	361 (97.3)	171 (99.4)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.8219 [0.2150, 15.4345] 0.5822
Stratified log-rank p-value [c]			0.5767

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Vascular disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	43 (11.6)	19 (11.0)	
Number of subjects censored, n (%)	328 (88.4)	153 (89.0)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.7361 [0.4215, 1.2853] 0.2813
Stratified log-rank p-value [c]			0.2819

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Vascular disorders; PT: Hypertension

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	14 (3.8)	7 (4.1)	
Number of subjects censored, n (%)	357 (96.2)	165 (95.9)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.7374 [0.2911, 1.8681] 0.5207
Stratified log-rank p-value [c]			0.5173

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.8.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Vascular disorders; PT: Hypotension

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	10 (2.7)	1 (0.6)	
Number of subjects censored, n (%)	361 (97.3)	171 (99.4)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			4.3869 [0.5559, 34.6207] 0.1607
Stratified log-rank p-value [c]			0.1258

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.8.1 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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SOC: Cardiac disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	35 (9.4)	12 (7.0)	
Number of subjects censored, n (%)	336 (90.6)	160 (93.0)	
Median time to first event (months) [a]	NE	NE	
95% Confidence Interval	[NE, NE]	[NE, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.8900
95% Confidence Interval			[0.4496, 1.7619]
p-value			0.7380
Stratified log-rank p-value [c]			0.7379

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Renal and urinary disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	28 (7.5)	8 (4.7)	
Number of subjects censored, n (%)	343 (92.5)	164 (95.3)	
Median time to first event (months) [a]	NE	NE	
95% Confidence Interval	[NE, NE]	[NE, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			1.2207
95% Confidence Interval			[0.5489, 2.7148]
p-value			0.6248
Stratified log-rank p-value [c]			0.6243

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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SOC: Hepatobiliary disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	25 (6.7)	7 (4.1)	
Number of subjects censored, n (%)	346 (93.3)	165 (95.9)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.0238 [0.4311, 2.4315] 0.9575
Stratified log-rank p-value [c]			0.9586

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Ear and labyrinth disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	21 (5.7)	4 (2.3)	
Number of subjects censored, n (%)	350 (94.3)	168 (97.7)	
Median time to first event (months) [a]	NE	NE	
95% Confidence Interval	[NE, NE]	[NE, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			1.3568
95% Confidence Interval			[0.4498, 4.0925]
p-value			0.5880
Stratified log-rank p-value [c]			0.5865

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Reproductive system and breast disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	20 (5.4)	4 (2.3)	
Number of subjects censored, n (%)	351 (94.6)	168 (97.7)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.4406 [0.4796, 4.3273] 0.5154
Stratified log-rank p-value [c]			0.5128

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.8.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.5580
HER2 IHC 1+	214	193 (90.2)	21 (9.8)	0.1 (0.1, 0.1)	100	66 (66.0)	34 (34.0)	0.9 (0.4, 2.2)	2.1575 (1.6255, 2.8636) <0.0001	<0.0001	
HER2 IHC 2+/ISH Negative	157	135 (86.0)	22 (14.0)	0.1 (0.1, 0.1)	72	51 (70.8)	21 (29.2)	0.5 (0.3, 1.6)	1.8830 (1.3609, 2.6054) 0.0001	0.0002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.9637
1	220	198 (90.0)	22 (10.0)	0.1 (0.1, 0.1)	94	66 (70.2)	28 (29.8)	0.6 (0.4, 1.5)	2.0800 (1.5692, 2.7570) <0.0001	<0.0001	
>=2	150	129 (86.0)	21 (14.0)	0.1 (0.1, 0.1)	78	51 (65.4)	27 (34.6)	1.1 (0.3, 4.9)	1.9713 (1.4211, 2.7345) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											
Yes	233	207 (88.8)	26 (11.2)	0.1 (0.1, 0.1)	112	74 (66.1)	38 (33.9)	0.6 (0.4, 1.4)	2.0610 (1.5761, 2.6950) <0.0001	<0.0001	0.8304
No	98	88 (89.8)	10 (10.2)	0.1 (0.1, 0.1)	43	30 (69.8)	13 (30.2)	0.8 (0.3, 2.7)	2.1548 (1.4152, 3.2810) 0.0003	0.0004	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2911
<65	289	255 (88.2)	34 (11.8)	0.1 (0.1, 0.1)	126	81 (64.3)	45 (35.7)	0.9 (0.5, 2.1)	2.1808 (1.6938, 2.8078) <0.0001	<0.0001	
>=65	82	73 (89.0)	9 (11.0)	0.1 (0.1, 0.1)	46	36 (78.3)	10 (21.7)	0.4 (0.2, 1.5)	1.7104 (1.1418, 2.5621) 0.0092	0.0120	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8411
<75	357	316 (88.5)	41 (11.5)	0.1 (0.1, 0.1)	163	111 (68.1)	52 (31.9)	0.6 (0.4, 1.4)	2.0365 (1.6367, 2.5340) <0.0001	<0.0001	
>=75	14	12 (85.7)	2 (14.3)	0.5 (0.1, 2.0)	9	6 (66.7)	3 (33.3)	4.9 (0.0, 11.7)	2.3004 (0.7948, 6.6578) 0.1244	0.1181	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.2333
White	175	151 (86.3)	24 (13.7)	0.1 (0.1, 0.1)	85	58 (68.2)	27 (31.8)	0.5 (0.4, 1.3)	1.7883 (1.3181, 2.4263) 0.0002	0.0002	
Non-White	196	177 (90.3)	19 (9.7)	0.1 (0.1, 0.1)	86	59 (68.6)	27 (31.4)	1.2 (0.3, 2.4)	2.2496 (1.6688, 3.0327) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.9541
Asia	147	131 (89.1)	16 (10.9)	0.1 (0.1, 0.1)	63	43 (68.3)	20 (31.7)	0.7 (0.3, 2.2)	2.1033 (1.4850, 2.9792) <0.0001	<0.0001	
North America	58	52 (89.7)	6 (10.3)	0.1 (0.1, 0.2)	28	20 (71.4)	8 (28.6)	0.5 (0.3, 1.4)	2.1848 (1.2841, 3.7171) 0.0039	0.0039	
Europe + Israel	166	145 (87.3)	21 (12.7)	0.1 (0.1, 0.1)	81	54 (66.7)	27 (33.3)	1.0 (0.4, 2.8)	1.9549 (1.4252, 2.6814) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											
0	199	177 (88.9)	22 (11.1)	0.1 (0.1, 0.1)	95	63 (66.3)	32 (33.7)	0.7 (0.4, 2.0)	2.1112 (1.5790, 2.8227) <0.0001	<0.0001	0.7385
1	172	151 (87.8)	21 (12.2)	0.1 (0.1, 0.1)	77	54 (70.1)	23 (29.9)	0.6 (0.3, 2.1)	1.9379 (1.4147, 2.6545) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.9284
0	60	50 (83.3)	10 (16.7)	0.1 (0.1, 0.2)	31	21 (67.7)	10 (32.3)	0.7 (0.2, 4.9)	1.6618 (0.9941, 2.7782) 0.0527	0.0560	
1	107	95 (88.8)	12 (11.2)	0.1 (0.1, 0.1)	48	34 (70.8)	14 (29.2)	0.7 (0.4, 1.6)	2.2033 (1.4807, 3.2784) 0.0001	<0.0001	
2	114	100 (87.7)	14 (12.3)	0.1 (0.1, 0.1)	50	32 (64.0)	18 (36.0)	1.2 (0.3, 5.4)	2.0933 (1.3989, 3.1324) 0.0003	0.0003	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 (92.2)	7 (7.8)	0.1 (0.1, 0.1)	43 (69.8)	13 (30.2)	0.5 (0.3, 2.0)	2.1812 (1.4294, 3.3285) 0.0003	0.0003	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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DE.T.4.8.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.1330
PD	173	150 (86.7)	23 (13.3)	0.1 (0.1, 0.1)	77	45 (58.4)	32 (41.6)	2.5 (1.1, 5.4)	2.4382 (1.7389, 3.4185)	<0.0001	
PR	48	41 (85.4)	7 (14.6)	0.1 (0.1, 0.2)	21	13 (61.9)	8 (38.1)	0.5 (0.2, NE)	2.1861 (1.1668, 4.0960)	0.0148	
SD	82	76 (92.7)	6 (7.3)	0.1 (0.1, 0.2)	54	44 (81.5)	10 (18.5)	0.5 (0.3, 0.8)	1.5689 (1.0790, 2.2811)	0.0215	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.5723
Yes	37	31 (83.8)	6 (16.2)	0.1 (0.1, 0.3)	13	10 (76.9)	3 (23.1)	0.8 (0.1, 2.8)	1.7650 (0.8579, 3.6309)	0.1249	
No	334	297 (88.9)	37 (11.1)	0.1 (0.1, 0.1)	159	107 (67.3)	52 (32.7)	0.6 (0.4, 1.6)	2.0655 (1.6521, 2.5824)	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.1214
Yes	24	17 (70.8)	7 (29.2)	0.2 (0.1, 1.5)	7	6 (85.7)	1 (14.3)	0.8 (0.1, 1.4)	0.9561 (0.3748, 2.4388)	0.9251	0.8970
No	347	311 (89.6)	36 (10.4)	0.1 (0.1, 0.1)	165	111 (67.3)	54 (32.7)	0.6 (0.5, 1.6)	2.1335 (1.7135, 2.6565)	<0.0001	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Gastrointestinal disorders; PT: Any PT

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.5833
Normal Function	201	172 (85.6)	29 (14.4)	0.1 (0.1, 0.1)	80	49 (61.3)	31 (38.8)	0.9 (0.5, 4.2)	2.1295 (1.5453, 2.9345) <0.0001	<0.0001	
Mild Impairment	123	115 (93.5)	8 (6.5)	0.1 (0.1, 0.1)	65	51 (78.5)	14 (21.5)	0.5 (0.3, 1.1)	2.0374 (1.4586, 2.8459) <0.0001	<0.0001	
Moderate Impairment	41	35 (85.4)	6 (14.6)	0.4 (0.1, 0.7)	23	16 (69.6)	7 (30.4)	1.2 (0.2, 11.7)	1.5291 (0.8402, 2.7828) 0.1645	0.1629	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.4005
Normal Function	170	153 (90.0)	17 (10.0)	0.1 (0.1, 0.1)	88	61 (69.3)	27 (30.7)	1.0 (0.4, 2.2)	2.1395 (1.5838, 2.8902) <0.0001	<0.0001	
Mild Impairment	194	168 (86.6)	26 (13.4)	0.1 (0.1, 0.1)	82	56 (68.3)	26 (31.7)	0.5 (0.3, 1.4)	1.8429 (1.3585, 2.5000) 0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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Baseline visceral disease											0.6889
Yes	331	292 (88.2)	39 (11.8)	0.1 (0.1, 0.1)	146	100 (68.5)	46 (31.5)	0.8 (0.4, 1.5)	2.0061 (1.5946, 2.5237) <0.0001	<0.0001	
No	40	36 (90.0)	4 (10.0)	0.1 (0.1, 0.1)	26	17 (65.4)	9 (34.6)	0.6 (0.3, 5.0)	2.1814 (1.2132, 3.9221) 0.0092	0.0098	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Hormon receptor status (IXRS)											0.3759
Positive	329	292 (88.8)	37 (11.2)	0.1 (0.1, 0.1)	152	101 (66.4)	51 (33.6)	0.7 (0.5, 1.5)	2.1059 (1.6752, 2.6472) <0.0001	<0.0001	
Negative	42	36 (85.7)	6 (14.3)	0.1 (0.1, 0.3)	20	16 (80.0)	4 (20.0)	0.6 (0.1, 4.9)	1.6246 (0.8955, 2.9470) 0.1103	0.1171	

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.6612
Positive	331	294 (88.8)	37 (11.2)	0.1 (0.1, 0.1)	155	104 (67.1)	51 (32.9)	0.6 (0.4, 1.5)	2.0756 (1.6557, 2.6021)	<0.0001	
Negative	40	34 (85.0)	6 (15.0)	0.1 (0.1, 0.3)	17	13 (76.5)	4 (23.5)	0.7 (0.1, 4.9)	1.7634 (0.9227, 3.3701)	0.0861	

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HER2 status											0.6089
HER2 IHC 1+	214	165 (77.1)	49 (22.9)	0.1 (0.1, 0.2)	100	29 (29.0)	71 (71.0)	NE (8.2, NE)	4.3135 (2.8994, 6.4175) <0.0001	<0.0001	
HER2 IHC 2+/ISH Negative	157	117 (74.5)	40 (25.5)	0.1 (0.1, 0.2)	72	23 (31.9)	49 (68.1)	NE (6.0, NE)	3.6065 (2.3004, 5.6541) <0.0001	<0.0001	

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	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting									0.4940
1	220 (76.8)	169 (23.2)	0.1 (0.1, 0.2)	94 (34.0)	32 (66.0)	NE (6.0, NE)	3.6871 (2.5201, 5.3943) <0.0001	<0.0001	
>=2	150 (74.7)	112 (25.3)	0.1 (0.1, 0.5)	78 (25.6)	20 (74.4)	NE (11.7, NE)	4.4688 (2.7701, 7.2090) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
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 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.5381
Yes	233	177 (76.0)	56 (24.0)	0.1 (0.1, 0.2)	112	34 (30.4)	78 (69.6)	NE (6.0, NE)	3.9116 (2.7037, 5.6591) <0.0001	<0.0001	
No	98	78 (79.6)	20 (20.4)	0.1 (0.1, 0.2)	43	12 (27.9)	31 (72.1)	NE (11.7, NE)	4.7305 (2.5655, 8.7227) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1084
<65	289	221 (76.5)	68 (23.5)	0.1 (0.1, 0.2)	126	33 (26.2)	93 (73.8)	NE (NE, NE)	4.6518 (3.2197, 6.7210) <0.0001	<0.0001	
>=65	82	61 (74.4)	21 (25.6)	0.2 (0.1, 0.7)	46	19 (41.3)	27 (58.7)	8.2 (1.7, NE)	2.8150 (1.6767, 4.7263) 0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:37; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_AESOCPT10PAT\_2\_SAS.rf

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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7437
<75	357	271 (75.9)	86 (24.1)	0.1 (0.1, 0.2)	163	50 (30.7)	113 (69.3)	NE (8.2, NE)	3.9508 (2.9164, 5.3521) <0.0001	<0.0001	
>=75	14	11 (78.6)	3 (21.4)	0.7 (0.1, 2.8)	9	2 (22.2)	7 (77.8)	NE (0.0, NE)	10.5178 (1.3442, 82.2980) 0.0250	0.0054	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.0427
White	175	127 (72.6)	48 (27.4)	0.2 (0.1, 0.4)	85	30 (35.3)	55 (64.7)	NE (NE, NE)	3.0306 (2.0316, 4.5209) <0.0001	<0.0001	
Non-White	196	155 (79.1)	41 (20.9)	0.1 (0.1, 0.1)	86	22 (25.6)	64 (74.4)	NE (8.2, NE)	5.2486 (3.3483, 8.2274) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.2863
Asia	147	113 (76.9)	34 (23.1)	0.1 (0.1, 0.1)	63	15 (23.8)	48 (76.2)	NE (11.7, NE)	5.1894 (3.0203, 8.9164) <0.0001	<0.0001	
North America	58	48 (82.8)	10 (17.2)	0.1 (0.1, 0.2)	28	9 (32.1)	19 (67.9)	6.0 (6.0, NE)	4.6129 (2.2451, 9.4780) <0.0001	<0.0001	
Europe + Israel	166	121 (72.9)	45 (27.1)	0.2 (0.1, 0.5)	81	28 (34.6)	53 (65.4)	NE (4.2, NE)	3.2174 (2.1273, 4.8662) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											
0	199	154 (77.4)	45 (22.6)	0.1 (0.1, 0.1)	95	28 (29.5)	67 (70.5)	NE (8.2, NE)	4.1483 (2.7666, 6.2200) <0.0001	<0.0001	0.7537
1	172	128 (74.4)	44 (25.6)	0.2 (0.1, 0.3)	77	24 (31.2)	53 (68.8)	NE (6.0, NE)	3.8116 (2.4575, 5.9120) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.8242
0	60	43 (71.7)	17 (28.3)	0.1 (0.1, 0.7)	31	10 (32.3)	21 (67.7)	NE (2.5, NE)	3.4966 (1.7492, 6.9896) 0.0004	0.0002	
1	107	83 (77.6)	24 (22.4)	0.1 (0.1, 0.2)	48	15 (31.3)	33 (68.8)	NE (8.2, NE)	4.3782 (2.5138, 7.6252) <0.0001	<0.0001	
2	114	83 (72.8)	31 (27.2)	0.1 (0.1, 0.5)	50	12 (24.0)	38 (76.0)	NE (6.0, NE)	4.6746 (2.5439, 8.5899) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 (81.1)	17 (18.9)	0.1 (0.1, 0.2)	43 (34.9)	28 (65.1)	11.7 (11.7, NE)	3.4482 (1.9723, 6.0286) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.8014
PD	173	127 (73.4)	46 (26.6)	0.2 (0.1, 0.3)	77	21 (27.3)	56 (72.7)	8.2 (6.0, NE)	4.1871 (2.6316, 6.6619)	<0.0001	
PR	48	37 (77.1)	11 (22.9)	0.1 (0.1, 0.3)	21	8 (38.1)	13 (61.9)	NE (0.3, NE)	3.1815 (1.4742, 6.8662)	0.0019	
SD	82	65 (79.3)	17 (20.7)	0.1 (0.1, 0.7)	54	18 (33.3)	36 (66.7)	NE (NE, NE)	3.7393 (2.2115, 6.3224)	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.5535
Yes	37	27 (73.0)	10 (27.0)	0.2 (0.1, 0.9)	13	5 (38.5)	8 (61.5)	NE (0.7, NE)	3.1148 (1.1917, 8.1410)	0.0147	
No	334	255 (76.3)	79 (23.7)	0.1 (0.1, 0.2)	159	47 (29.6)	112 (70.4)	NE (8.2, NE)	4.0942 (2.9937, 5.5994)	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.6652
Yes	24	14 (58.3)	10 (41.7)	1.1 (0.1, NE)	7	2 (28.6)	5 (71.4)	NE (0.1, NE)	2.7492 (0.6225, 12.1406) 0.1820	0.1594	
No	347	268 (77.2)	79 (22.8)	0.1 (0.1, 0.2)	165	50 (30.3)	115 (69.7)	NE (8.2, NE)	4.1116 (3.0339, 5.5720) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.4545
Normal Function	201	155 (77.1)	46 (22.9)	0.1 (0.1, 0.1)	80	22 (27.5)	58 (72.5)	NE (NE, NE)	4.6275 (2.9521, 7.2536) <0.0001	<0.0001	
Mild Impairment	123	93 (75.6)	30 (24.4)	0.1 (0.1, 0.2)	65	23 (35.4)	42 (64.6)	NE (2.5, NE)	3.2001 (2.0217, 5.0653) <0.0001	<0.0001	
Moderate Impairment	41	28 (68.3)	13 (31.7)	0.7 (0.2, 2.1)	23	7 (30.4)	16 (69.6)	NE (8.2, NE)	3.3541 (1.4562, 7.7257) 0.0045	0.0026	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.3340
Normal Function	170	133 (78.2)	37 (21.8)	0.1 (0.1, 0.1)	88	26 (29.5)	62 (70.5)	NE (11.7, NE)	4.5380 (2.9706, 6.9325) <0.0001	<0.0001	
Mild Impairment	194	143 (73.7)	51 (26.3)	0.2 (0.1, 0.3)	82	26 (31.7)	56 (68.3)	NE (8.2, NE)	3.3822 (2.2227, 5.1465) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.8902
Yes	331	252 (76.1)	79 (23.9)	0.1 (0.1, 0.2)	146	44 (30.1)	102 (69.9)	NE (8.2, NE)	4.0459 (2.9312, 5.5845) <0.0001	<0.0001	
No	40	30 (75.0)	10 (25.0)	0.1 (0.1, 0.8)	26	8 (30.8)	18 (69.2)	NE (0.7, NE)	3.7644 (1.7188, 8.2444) 0.0009	0.0004	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.7830
Positive	329	253 (76.9)	76 (23.1)	0.1 (0.1, 0.2)	152	46 (30.3)	106 (69.7)	NE (11.7, NE)	4.0525 (2.9540, 5.5593) <0.0001	<0.0001	
Negative	42	29 (69.0)	13 (31.0)	0.2 (0.1, 0.7)	20	6 (30.0)	14 (70.0)	NE (0.9, NE)	3.6022 (1.4876, 8.7228) 0.0045	0.0026	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.5814
Positive	331	254 (76.7)	77 (23.3)	0.1 (0.1, 0.2)	155	46 (29.7)	109 (70.3)	NE (11.7, NE)	4.1108 (2.9969, 5.6387)	<0.0001	
Negative	40	28 (70.0)	12 (30.0)	0.2 (0.1, 0.7)	17	6 (35.3)	11 (64.7)	NE (0.7, NE)	3.1976 (1.3165, 7.7661)	0.0071	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Vomiting

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.9599
HER2 IHC 1+	214	83 (38.8)	131 (61.2)	NE (10.6, NE)	100	13 (13.0)	87 (87.0)	NE (NE, NE)	3.2186 (1.7904, 5.7861) 0.0001	<0.0001	
HER2 IHC 2+/ISH Negative	157	67 (42.7)	90 (57.3)	NE (5.7, NE)	72	10 (13.9)	62 (86.1)	NE (NE, NE)	3.1418 (1.6143, 6.1145) 0.0008	0.0004	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Vomiting

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.0786
1	220	92 (41.8)	128 (58.2)	NE (9.3, NE)	94	9 (9.6)	85 (90.4)	NE (NE, NE)	4.7353 (2.3854, 9.4003) <0.0001	<0.0001	
>=2	150	57 (38.0)	93 (62.0)	NE (10.9, NE)	78	14 (17.9)	64 (82.1)	NE (6.8, NE)	2.1761 (1.2100, 3.9136) 0.0094	0.0079	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Vomiting

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											
Yes	233	85 (36.5)	148 (63.5)	NE (10.6, NE)	112	14 (12.5)	98 (87.5)	NE (NE, NE)	2.8393 (1.6073, 5.0157) 0.0003	0.0002	0.1158
No	98	52 (53.1)	46 (46.9)	5.4 (1.4, NE)	43	4 (9.3)	39 (90.7)	NE (NE, NE)	7.1297 (2.5773, 19.7232) 0.0002	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Vomiting

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5104
<65	289	120 (41.5)	169 (58.5)	NE (9.5, NE)	126	16 (12.7)	110 (87.3)	NE (NE, NE)	3.4830 (2.0648, 5.8752) <0.0001	<0.0001	
>=65	82	30 (36.6)	52 (63.4)	NE (5.7, NE)	46	7 (15.2)	39 (84.8)	NE (NE, NE)	2.3928 (1.0476, 5.4653) 0.0384	0.0334	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Vomiting

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2771
<75	357	147 (41.2)	210 (58.8)	NE (10.3, NE)	163	23 (14.1)	140 (85.9)	NE (NE, NE)	3.0804 (1.9823, 4.7866) <0.0001	<0.0001	
>=75	14	3 (21.4)	11 (78.6)	NE (5.6, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9974	0.1697	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Run date: 13SEP2022 – 17:37; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_AESOCPT10PAT\_2\_SAS.rf

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SOC: Gastrointestinal disorders; PT: Vomiting

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.4686
White	175	72 (41.1)	103 (58.9)	NE (9.5, NE)	85	13 (15.3)	72 (84.7)	NE (NE, NE)	2.6613 (1.4689, 4.8216) 0.0012	0.0008	
Non-White	196	78 (39.8)	118 (60.2)	NE (9.3, NE)	86	10 (11.6)	76 (88.4)	NE (NE, NE)	3.7848 (1.9580, 7.3158) 0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Vomiting

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.4645
Asia	147	57 (38.8)	90 (61.2)	NE (10.9, NE)	63	7 (11.1)	56 (88.9)	NE (NE, NE)	3.8404 (1.7502, 8.4267) 0.0008	0.0003	
North America	58	28 (48.3)	30 (51.7)	10.6 (0.9, NE)	28	3 (10.7)	25 (89.3)	NE (6.0, NE)	4.8671 (1.4704, 16.1108) 0.0096	0.0042	
Europe + Israel	166	65 (39.2)	101 (60.8)	NE (9.5, NE)	81	13 (16.0)	68 (84.0)	NE (NE, NE)	2.4214 (1.3309, 4.4054) 0.0038	0.0028	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Vomiting

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											
0	199	74 (37.2)	125 (62.8)	NE (12.1, NE)	95	7 (7.4)	88 (92.6)	NE (NE, NE)	5.0716 (2.3332, 11.0240) <0.0001	<0.0001	0.1028
1	172	76 (44.2)	96 (55.8)	10.9 (5.0, NE)	77	16 (20.8)	61 (79.2)	NE (6.8, NE)	2.3637 (1.3758, 4.0609) 0.0018	0.0014	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Vomiting

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.2505
0	60	20 (33.3)	40 (66.7)	NE (5.1, NE)	31	6 (19.4)	25 (80.6)	NE (NE, NE)	1.6797 (0.6740, 4.1858) 0.2656	0.2597	
1	107	42 (39.3)	65 (60.7)	NE (9.3, NE)	48	8 (16.7)	40 (83.3)	NE (NE, NE)	2.6555 (1.2450, 5.6642) 0.0115	0.0089	
2	114	60 (52.6)	54 (47.4)	5.4 (2.1, NE)	50	5 (10.0)	45 (90.0)	NE (6.0, NE)	5.7729 (2.3135, 14.4053) 0.0002	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Vomiting

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 (31.1)	62 (68.9)	NE (12.1, NE)	43 (9.3)	39 (90.7)	NE (NE, NE)	3.2188 (1.1227, 9.2282) 0.0296	0.0215	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Vomiting

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.3455
PD	173	72 (41.6)	101 (58.4)	NE (5.6, NE)	77	10 (13.0)	67 (87.0)	NE (NE, NE)	3.3876 (1.7460, 6.5729) 0.0003	0.0001	
PR	48	14 (29.2)	34 (70.8)	NE (NE, NE)	21	4 (19.0)	17 (81.0)	NE (NE, NE)	1.4401 (0.4726, 4.3887) 0.5212	0.5196	
SD	82	36 (43.9)	46 (56.1)	12.1 (4.3, NE)	54	7 (13.0)	47 (87.0)	NE (NE, NE)	3.6404 (1.6162, 8.2000) 0.0018	0.0009	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Gastrointestinal disorders; PT: Vomiting

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.2589
Yes	37	13 (35.1)	24 (64.9)	NE (1.5, NE)	13	3 (23.1)	10 (76.9)	6.8 (0.8, NE)	1.5526 (0.4409, 5.4678) 0.4934	0.4895	
No	334	137 (41.0)	197 (59.0)	NE (10.4, NE)	159	20 (12.6)	139 (87.4)	NE (NE, NE)	3.4402 (2.1494, 5.5061) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.4391
Yes	24	10 (41.7)	14 (58.3)	NE (0.8, NE)	7	2 (28.6)	5 (71.4)	6.8 (0.8, NE)	1.7593 (0.3843, 8.0541) 0.4667	0.4568	
No	347	140 (40.3)	207 (59.7)	NE (10.4, NE)	165	21 (12.7)	144 (87.3)	NE (NE, NE)	3.3112 (2.0906, 5.2443) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Vomiting

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.5820
Normal Function	201	87 (43.3)	114 (56.7)	12.1 (8.3, NE)	80	10 (12.5)	70 (87.5)	NE (NE, NE)	3.7839 (1.9638, 7.2909) 0.0001	<0.0001	
Mild Impairment	123	40 (32.5)	83 (67.5)	NE (NE, NE)	65	9 (13.8)	56 (86.2)	NE (NE, NE)	2.3122 (1.1186, 4.7796) 0.0237	0.0201	
Moderate Impairment	41	19 (46.3)	22 (53.7)	10.9 (1.0, NE)	23	4 (17.4)	19 (82.6)	NE (6.8, NE)	2.9139 (0.9906, 8.5712) 0.0520	0.0419	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Vomiting

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.5707
Normal Function	170	77 (45.3)	93 (54.7)	12.1 (5.7, NE)	88	15 (17.0)	73 (83.0)	NE (NE, NE)	2.8846 (1.6565, 5.0229) 0.0002	<0.0001	
Mild Impairment	194	69 (35.6)	125 (64.4)	NE (10.4, NE)	82	8 (9.8)	74 (90.2)	NE (NE, NE)	3.6781 (1.7649, 7.6651) 0.0005	0.0002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Vomiting

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.0758
Yes	331	131 (39.6)	200 (60.4)	NE (12.1, NE)	146	16 (11.0)	130 (89.0)	NE (NE, NE)	3.9479 (2.3473, 6.6399) <0.0001	<0.0001	
No	40	19 (47.5)	21 (52.5)	10.4 (1.7, NE)	26	7 (26.9)	19 (73.1)	NE (NE, NE)	1.4200 (0.5872, 3.4343) 0.4364	0.4355	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Vomiting

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.1061
Positive	329	135 (41.0)	194 (59.0)	NE (10.4, NE)	152	18 (11.8)	134 (88.2)	NE (NE, NE)	3.6870 (2.2521, 6.0362) <0.0001	<0.0001	
Negative	42	15 (35.7)	27 (64.3)	NE (3.4, NE)	20	5 (25.0)	15 (75.0)	NE (0.9, NE)	1.3684 (0.4954, 3.7796) 0.5451	0.5407	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Vomiting

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.0255
Positive	331	138 (41.7)	193 (58.3)	NE (10.4, NE)	155	18 (11.6)	137 (88.4)	NE (NE, NE)	3.8448 (2.3501, 6.2901)	<0.0001	
Negative	40	12 (30.0)	28 (70.0)	NE (5.1, NE)	17	5 (29.4)	12 (70.6)	NE (0.7, NE)	0.9018 (0.3152, 2.5796)	0.8496	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Constipation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.4002
HER2 IHC 1+	214	68 (31.8)	146 (68.2)	NE (17.3, NE)	100	23 (23.0)	77 (77.0)	NE (6.5, NE)	1.1934 (0.7407, 1.9229) 0.4676	0.4704	
HER2 IHC 2+/ISH Negative	157	58 (36.9)	99 (63.1)	NE (11.2, NE)	72	15 (20.8)	57 (79.2)	NE (7.6, NE)	1.6323 (0.9214, 2.8917) 0.0931	0.0903	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Constipation

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting									0.8356
1	220 (33.6)	74 (33.6)	146 (66.4) NE (17.3, NE)	94 (23.4)	22 (23.4)	72 (76.6) NE (7.6, NE)	1.2954 (0.8017, 2.0933) 0.2904	0.2927	
>=2	150 (34.0)	51 (34.0)	99 (66.0) NE (14.6, NE)	78 (20.5)	16 (20.5)	62 (79.5) NE (NE, NE)	1.4795 (0.8407, 2.6035) 0.1744	0.1715	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.9287
Yes	233	81 (34.8)	152 (65.2)	NE (16.5, NE)	112	26 (23.2)	86 (76.8)	10.9 (6.5, NE)	1.3488 (0.8636, 2.1069)	0.1884	0.1890
No	98	31 (31.6)	67 (68.4)	NE (14.6, NE)	43	9 (20.9)	34 (79.1)	NE (NE, NE)	1.2982 (0.6155, 2.7382)	0.4931	0.4935

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Gastrointestinal disorders; PT: Constipation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8001
<65	289	97 (33.6)	192 (66.4)	NE (17.3, NE)	126	26 (20.6)	100 (79.4)	NE (7.6, NE)	1.4309 (0.9247, 2.2142) 0.1077	0.1067	
>=65	82	29 (35.4)	53 (64.6)	NE (11.5, NE)	46	12 (26.1)	34 (73.9)	NE (5.3, NE)	1.2888 (0.6553, 2.5350) 0.4622	0.4657	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6456
<75	357	123 (34.5)	234 (65.5)	NE (17.3, NE)	163	36 (22.1)	127 (77.9)	NE (10.9, NE)	1.3865 (0.9532, 2.0166) 0.0874	0.0874	
>=75	14	3 (21.4)	11 (78.6)	NE (4.1, NE)	9	2 (22.2)	7 (77.8)	NE (0.1, NE)	0.8521 (0.1419, 5.1168) 0.8611	0.8609	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.0808
White	175	50 (28.6)	125 (71.4)	NE (17.3, NE)	85	21 (24.7)	64 (75.3)	NE (6.5, NE)	0.9395 (0.5602, 1.5758) 0.8131	0.8105	
Non-White	196	76 (38.8)	120 (61.2)	NE (11.2, NE)	86	17 (19.8)	69 (80.2)	NE (10.9, NE)	1.9125 (1.1279, 3.2428) 0.0161	0.0144	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Constipation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.0475
Asia	147	57 (38.8)	90 (61.2)	NE (11.2, NE)	63	10 (15.9)	53 (84.1)	NE (10.9, NE)	2.3449 (1.1934, 4.6075) 0.0134	0.0110	
North America	58	25 (43.1)	33 (56.9)	11.5 (3.7, NE)	28	7 (25.0)	21 (75.0)	7.6 (5.7, NE)	1.6353 (0.7003, 3.8185) 0.2557	0.2529	
Europe + Israel	166	44 (26.5)	122 (73.5)	NE (NE, NE)	81	21 (25.9)	60 (74.1)	NE (6.5, NE)	0.8437 (0.4990, 1.4263) 0.5257	0.5242	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Constipation

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	199	70 (35.2)	129 (64.8)	NE (16.5, NE)	95	17 (17.9)	78 (82.1)	NE (10.9, NE)	1.7410 (1.0215, 2.9674) 0.0415	0.0394	0.1952
1	172	56 (32.6)	116 (67.4)	NE (17.3, NE)	77	21 (27.3)	56 (72.7)	NE (6.5, NE)	1.0855 (0.6541, 1.8013) 0.7509	0.7625	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Constipation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.0158
0	60	20 (33.3)	40 (66.7)	NE (14.6, NE)	31	7 (22.6)	24 (77.4)	NE (5.3, NE)	1.3435 (0.5661, 3.1881) 0.5031	0.5064	
1	107	28 (26.2)	79 (73.8)	NE (16.5, NE)	48	14 (29.2)	34 (70.8)	NE (6.5, NE)	0.8492 (0.4457, 1.6182) 0.6193	0.6114	
2	114	38 (33.3)	76 (66.7)	NE (17.3, NE)	50	13 (26.0)	37 (74.0)	NE (5.7, NE)	1.0676 (0.5650, 2.0173) 0.8402	0.8377	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Constipation

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 (44.4)	50 (55.6)	10.8 (4.8, NE)	43 (9.3)	39 (90.7)	NE (10.9, NE)	4.4733 (1.5923, 12.5673) 0.0045	0.0019	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Constipation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.6789
PD	173	51 (29.5)	122 (70.5)	NE (NE, NE)	77	17 (22.1)	60 (77.9)	NE (7.6, NE)	1.1422 (0.6552, 1.9912) 0.6392	0.6469	
PR	48	17 (35.4)	31 (64.6)	17.3 (10.5, NE)	21	3 (14.3)	18 (85.7)	NE (NE, NE)	1.8745 (0.5420, 6.4831) 0.3209	0.3132	
SD	82	28 (34.1)	54 (65.9)	NE (14.6, NE)	54	14 (25.9)	40 (74.1)	NE (6.5, NE)	1.1857 (0.6196, 2.2690) 0.6069	0.6107	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Gastrointestinal disorders; PT: Constipation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.5378
Yes	37	18 (48.6)	19 (51.4)	4.2 (0.8, NE)	13	3 (23.1)	10 (76.9)	NE (0.8, NE)	1.9022 (0.5570, 6.4962) 0.3048	0.2954	
No	334	108 (32.3)	226 (67.7)	NE (NE, NE)	159	35 (22.0)	124 (78.0)	NE (10.9, NE)	1.3022 (0.8864, 1.9130) 0.1784	0.1805	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Constipation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.9566
Yes	24	10 (41.7)	14 (58.3)	NE (0.7, NE)	7	2 (28.6)	5 (71.4)	NE (0.1, NE)	1.3998 (0.3021, 6.4863) 0.6673	0.6714	
No	347	116 (33.4)	231 (66.6)	NE (NE, NE)	165	36 (21.8)	129 (78.2)	NE (10.9, NE)	1.3570 (0.9308, 1.9785) 0.1125	0.1129	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Constipation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.7745
Normal Function	201	68 (33.8)	133 (66.2)	NE (14.6, NE)	80	20 (25.0)	60 (75.0)	NE (10.9, NE)	1.1728 (0.7088, 1.9405) 0.5351	0.5392	
Mild Impairment	123	45 (36.6)	78 (63.4)	NE (11.2, NE)	65	14 (21.5)	51 (78.5)	NE (6.5, NE)	1.5717 (0.8591, 2.8754) 0.1423	0.1398	
Moderate Impairment	41	11 (26.8)	30 (73.2)	NE (16.5, NE)	23	4 (17.4)	19 (82.6)	NE (NE, NE)	1.4220 (0.4504, 4.4898) 0.5484	0.5455	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Constipation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.3502
Normal Function	170	64 (37.6)	106 (62.4)	NE (14.6, NE)	88	19 (21.6)	69 (78.4)	NE (10.9, NE)	1.5729 (0.9383, 2.6366) 0.0857	0.0842	
Mild Impairment	194	61 (31.4)	133 (68.6)	NE (NE, NE)	82	19 (23.2)	63 (76.8)	NE (6.5, NE)	1.2169 (0.7247, 2.0433) 0.4578	0.4563	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Constipation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.7607
Yes	331	111 (33.5)	220 (66.5)	NE (17.3, NE)	146	33 (22.6)	113 (77.4)	NE (10.9, NE)	1.3488 (0.9122, 1.9946) 0.1338	0.1334	
No	40	15 (37.5)	25 (62.5)	NE (5.7, NE)	26	5 (19.2)	21 (80.8)	NE (2.8, NE)	1.4786 (0.5244, 4.1696) 0.4596	0.4588	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Constipation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.9543
Positive	329	111 (33.7)	218 (66.3)	NE (17.3, NE)	152	33 (21.7)	119 (78.3)	NE (10.9, NE)	1.3763 (0.9301, 2.0363) 0.1101	0.1100	
Negative	42	15 (35.7)	27 (64.3)	NE (3.5, NE)	20	5 (25.0)	15 (75.0)	NE (2.0, NE)	1.3820 (0.5006, 3.8149) 0.5323	0.5375	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Constipation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.4995
Positive	331	111 (33.5)	220 (66.5)	NE (17.3, NE)	155	35 (22.6)	120 (77.4)	NE (10.9, NE)	1.3108 (0.8936, 1.9229) 0.1662	0.1669	
Negative	40	15 (37.5)	25 (62.5)	NE (3.5, NE)	17	3 (17.6)	14 (82.4)	NE (NE, NE)	2.1181 (0.6109, 7.3437) 0.2367	0.2286	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Diarrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0401
HER2 IHC 1+	214	57 (26.6)	157 (73.4)	NE (NE, NE)	100	28 (28.0)	72 (72.0)	NE (7.1, NE)	0.7888 (0.4989, 1.2471) 0.3101	0.3092	
HER2 IHC 2+/ISH Negative	157	43 (27.4)	114 (72.6)	NE (NE, NE)	72	10 (13.9)	62 (86.1)	NE (NE, NE)	1.8292 (0.9157, 3.6539) 0.0872	0.0828	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Diarrhoea

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting									0.9025
1	220	59 (26.8)	161 (73.2) NE (NE, NE)	94	21 (22.3)	73 (77.7) NE (NE, NE)	1.0858 (0.6581, 1.7915) 0.7472	0.7488	
>=2	150	41 (27.3)	109 (72.7) NE (13.9, NE)	78	17 (21.8)	61 (78.2) NE (NE, NE)	1.0596 (0.5984, 1.8762) 0.8426	0.8458	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Gastrointestinal disorders; PT: Diarrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.9946
Yes	233	72 (30.9)	161 (69.1)	NE (NE, NE)	112	26 (23.2)	86 (76.8)	NE (NE, NE)	1.1554 (0.7349, 1.8165) 0.5315	0.5311	
No	98	18 (18.4)	80 (81.6)	NE (NE, NE)	43	6 (14.0)	37 (86.0)	NE (NE, NE)	1.1284 (0.4452, 2.8601) 0.7990	0.8010	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Diarrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4563
<65	289	76 (26.3)	213 (73.7)	NE (NE, NE)	126	24 (19.0)	102 (81.0)	NE (NE, NE)	1.1963 (0.7532, 1.9000) 0.4477	0.4479	
>=65	82	24 (29.3)	58 (70.7)	NE (13.9, NE)	46	14 (30.4)	32 (69.6)	NE (7.1, NE)	0.8860 (0.4562, 1.7209) 0.7208	0.7146	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Gastrointestinal disorders; PT: Diarrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8304
<75	357	96 (26.9)	261 (73.1)	NE (NE, NE)	163	35 (21.5)	128 (78.5)	NE (NE, NE)	1.0839 (0.7336, 1.6014) 0.6859	0.6882	
>=75	14	4 (28.6)	10 (71.4)	NE (0.3, NE)	9	3 (33.3)	6 (66.7)	NE (0.4, NE)	0.9293 (0.2076, 4.1608) 0.9237	0.9236	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.4413
White	175	59 (33.7)	116 (66.3)	NE (NE, NE)	85	21 (24.7)	64 (75.3)	NE (NE, NE)	1.2516 (0.7584, 2.0657) 0.3799	0.3830	
Non-White	196	41 (20.9)	155 (79.1)	NE (NE, NE)	86	17 (19.8)	69 (80.2)	NE (NE, NE)	0.8847 (0.4993, 1.5674) 0.6745	0.6725	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.0631
Asia	147	24 (16.3)	123 (83.7)	NE (NE, NE)	63	14 (22.2)	49 (77.8)	NE (NE, NE)	0.5876 (0.3014, 1.1457) 0.1186	0.1143	
North America	58	23 (39.7)	35 (60.3)	NE (1.5, NE)	28	5 (17.9)	23 (82.1)	NE (NE, NE)	2.2558 (0.8534, 5.9625) 0.1009	0.0941	
Europe + Israel	166	53 (31.9)	113 (68.1)	NE (13.9, NE)	81	19 (23.5)	62 (76.5)	NE (7.1, NE)	1.2371 (0.7302, 2.0961) 0.4289	0.4303	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.8327
0	199	50 (25.1)	149 (74.9)	NE (NE, NE)	95	20 (21.1)	75 (78.9)	NE (NE, NE)	1.0785 (0.6398, 1.8181) 0.7765	0.7820	
1	172	50 (29.1)	122 (70.9)	NE (13.9, NE)	77	18 (23.4)	59 (76.6)	NE (NE, NE)	1.0632 (0.6170, 1.8320) 0.8253	0.8222	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Diarrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.2094
0	60	14 (23.3)	46 (76.7)	NE (NE, NE)	31	7 (22.6)	24 (77.4)	NE (4.9, NE)	0.8952 (0.3582, 2.2372) 0.8127	0.8080	
1	107	20 (18.7)	87 (81.3)	NE (NE, NE)	48	11 (22.9)	37 (77.1)	NE (NE, NE)	0.6767 (0.3231, 1.4173) 0.3005	0.2986	
2	114	42 (36.8)	72 (63.2)	NE (13.9, NE)	50	9 (18.0)	41 (82.0)	NE (NE, NE)	1.9865 (0.9630, 4.0975) 0.0632	0.0587	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Diarrhoea

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 (26.7)	66 (73.3)	NE (NE, NE)	43 (25.6)	32 (74.4)	NE (NE, NE)	0.8739 (0.4243, 1.7998) 0.7146	0.7100	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Diarrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.0578
PD	173	52 (30.1)	121 (69.9)	NE (13.9, NE)	77	11 (14.3)	66 (85.7)	NE (NE, NE)	1.8950 (0.9836, 3.6512) 0.0561	0.0526	
PR	48	8 (16.7)	40 (83.3)	NE (NE, NE)	21	5 (23.8)	16 (76.2)	NE (5.0, NE)	0.5375 (0.1723, 1.6767) 0.2849	0.2782	
SD	82	25 (30.5)	57 (69.5)	NE (10.4, NE)	54	17 (31.5)	37 (68.5)	NE (NE, NE)	0.8292 (0.4457, 1.5428) 0.5544	0.5543	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Diarrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.3693
Yes	37	8 (21.6)	29 (78.4)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	2.4222 (0.3004, 19.5332)	0.4062	0.3859
No	334	92 (27.5)	242 (72.5)	NE (NE, NE)	159	37 (23.3)	122 (76.7)	NE (NE, NE)	1.0394 (0.7074, 1.5270)	0.8441	0.8461

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Diarrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.7823
Yes	24	5 (20.8)	19 (79.2)	NE (9.5, NE)	7	1 (14.3)	6 (85.7)	NE (0.1, NE)	1.2574 (0.1451, 10.9002) 0.8353	0.8236	
No	347	95 (27.4)	252 (72.6)	NE (NE, NE)	165	37 (22.4)	128 (77.6)	NE (NE, NE)	1.0647 (0.7260, 1.5616) 0.7482	0.7510	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Diarrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.8478
Normal Function	201	52 (25.9)	149 (74.1)	NE (NE, NE)	80	16 (20.0)	64 (80.0)	NE (NE, NE)	1.1176 (0.6351, 1.9665) 0.6998	0.7031	
Mild Impairment	123	36 (29.3)	87 (70.7)	NE (NE, NE)	65	14 (21.5)	51 (78.5)	NE (NE, NE)	1.2128 (0.6494, 2.2651) 0.5449	0.5449	
Moderate Impairment	41	12 (29.3)	29 (70.7)	NE (13.9, NE)	23	7 (30.4)	16 (69.6)	NE (7.1, NE)	0.8963 (0.3527, 2.2776) 0.8180	0.8193	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Gastrointestinal disorders; PT: Diarrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.7760
Normal Function	170	54 (31.8)	116 (68.2)	NE (NE, NE)	88	22 (25.0)	66 (75.0)	NE (NE, NE)	1.1197 (0.6794, 1.8454) 0.6574	0.6591	
Mild Impairment	194	44 (22.7)	150 (77.3)	NE (NE, NE)	82	16 (19.5)	66 (80.5)	NE (7.1, NE)	1.0058 (0.5646, 1.7918) 0.9844	0.9883	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Diarrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.7610
Yes	331	89 (26.9)	242 (73.1)	NE (NE, NE)	146	32 (21.9)	114 (78.1)	NE (NE, NE)	1.0978 (0.7310, 1.6488) 0.6530	0.6561	
No	40	11 (27.5)	29 (72.5)	NE (NE, NE)	26	6 (23.1)	20 (76.9)	NE (5.0, NE)	0.9300 (0.3400, 2.5436) 0.8876	0.8881	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Gastrointestinal disorders; PT: Diarrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.3425
Positive	329	89 (27.1)	240 (72.9)	NE (NE, NE)	152	31 (20.4)	121 (79.6)	NE (NE, NE)	1.1562 (0.7660, 1.7452) 0.4895	0.4894	
Negative	42	11 (26.2)	31 (73.8)	NE (NE, NE)	20	7 (35.0)	13 (65.0)	5.0 (2.8, NE)	0.7116 (0.2740, 1.8476) 0.4845	0.4735	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Diarrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.3049
Positive	331	90 (27.2)	241 (72.8)	NE (NE, NE)	155	32 (20.6)	123 (79.4)	NE (NE, NE)	1.1558 (0.7700, 1.7349)	0.4854	
Negative	40	10 (25.0)	30 (75.0)	NE (NE, NE)	17	6 (35.3)	11 (64.7)	4.9 (2.8, NE)	0.5725 (0.2000, 1.6386)	0.2863	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.6750
HER2 IHC 1+	214	24 (11.2)	190 (88.8)	NE (NE, NE)	100	11 (11.0)	89 (89.0)	NE (11.3, NE)	0.7383 (0.3574, 1.5251) 0.4124	0.4115	
HER2 IHC 2+/ISH Negative	157	17 (10.8)	140 (89.2)	NE (NE, NE)	72	6 (8.3)	66 (91.7)	NE (NE, NE)	0.9931 (0.3882, 2.5405) 0.9885	0.9891	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting									0.7885
1	220	24 (10.9)	196 (89.1)	94	10 (10.6)	84 (89.4)	0.7887 (0.3735, 1.6655) 0.5337	0.5334	
>=2	150	17 (11.3)	133 (88.7)	78	7 (9.0)	71 (91.0)	0.8503 (0.3470, 2.0839) 0.7230	0.7231	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.5169
Yes	233	25 (10.7)	208 (89.3)	NE (NE, NE)	112	13 (11.6)	99 (88.4)	NE (NE, NE)	0.7015 (0.3552, 1.3853) 0.3072	0.3055	
No	98	12 (12.2)	86 (87.8)	NE (NE, NE)	43	4 (9.3)	39 (90.7)	NE (11.3, NE)	0.9036 (0.2880, 2.8351) 0.8620	0.8620	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6472
<65	289	28 (9.7)	261 (90.3)	NE (NE, NE)	126	9 (7.1)	117 (92.9)	NE (11.3, NE)	0.9957 (0.4650, 2.1322) 0.9911	0.9911	
>=65	82	13 (15.9)	69 (84.1)	NE (NE, NE)	46	8 (17.4)	38 (82.6)	NE (NE, NE)	0.7056 (0.2895, 1.7197) 0.4429	0.4439	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6956
<75	357	39 (10.9)	318 (89.1)	NE (NE, NE)	163	16 (9.8)	147 (90.2)	NE (NE, NE)	0.7923 (0.4381, 1.4330) 0.4413	0.4406	
>=75	14	2 (14.3)	12 (85.7)	NE (3.8, NE)	9	1 (11.1)	8 (88.9)	NE (0.6, NE)	1.3370 (0.1211, 14.7574) 0.8126	0.8120	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.9911
White	175	14 (8.0)	161 (92.0)	NE (NE, NE)	85	6 (7.1)	79 (92.9)	NE (NE, NE)	0.8993 (0.3418, 2.3661) 0.8297	0.8299	
Non-White	196	27 (13.8)	169 (86.2)	NE (NE, NE)	86	11 (12.8)	75 (87.2)	NE (11.3, NE)	0.7734 (0.3798, 1.5747) 0.4787	0.4778	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.5530
Asia	147	23 (15.6)	124 (84.4)	NE (NE, NE)	63	7 (11.1)	56 (88.9)	NE (NE, NE)	1.0000 (0.4251, 2.3523) 1.0000	0.9993	
North America	58	6 (10.3)	52 (89.7)	NE (NE, NE)	28	2 (7.1)	26 (92.9)	NE (NE, NE)	1.1876 (0.2385, 5.9140) 0.8338	0.8336	
Europe + Israel	166	12 (7.2)	154 (92.8)	NE (NE, NE)	81	8 (9.9)	73 (90.1)	NE (11.3, NE)	0.5416 (0.2168, 1.3530) 0.1892	0.1828	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											
0	199	19 (9.5)	180 (90.5)	NE (NE, NE)	95	9 (9.5)	86 (90.5)	NE (NE, NE)	0.7337 (0.3286, 1.6384) 0.4500	0.4493	0.6149
1	172	22 (12.8)	150 (87.2)	NE (NE, NE)	77	8 (10.4)	69 (89.6)	NE (11.3, NE)	0.9036 (0.3954, 2.0647) 0.8099	0.8100	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.6289
0	60	5 (8.3)	55 (91.7)	NE (NE, NE)	31	3 (9.7)	28 (90.3)	NE (NE, NE)	0.5720 (0.1313, 2.4920) 0.4569	0.4518	
1	107	12 (11.2)	95 (88.8)	NE (NE, NE)	48	3 (6.3)	45 (93.8)	NE (NE, NE)	1.6017 (0.4497, 5.7052) 0.4674	0.4642	
2	114	10 (8.8)	104 (91.2)	NE (NE, NE)	50	5 (10.0)	45 (90.0)	11.3 (11.3, NE)	0.6217 (0.2088, 1.8507) 0.3931	0.3895	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 (15.6)	76 (84.4)	NE (NE, NE)	43 (14.0)	6 (86.0)	NE (NE, NE)	0.6871 (0.2572, 1.8353) 0.4540	0.4534	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.9415
PD	173	15 (8.7)	158 (91.3)	NE (NE, NE)	77	6 (7.8)	71 (92.2)	11.3 (11.3, NE)	0.8044 (0.3077, 2.1029)	0.6554	
PR	48	5 (10.4)	43 (89.6)	NE (NE, NE)	21	2 (9.5)	19 (90.5)	NE (NE, NE)	0.6571 (0.0984, 3.2030)	0.5106	
SD	82	13 (15.9)	69 (84.1)	NE (NE, NE)	54	7 (13.0)	47 (87.0)	NE (NE, NE)	0.9177 (0.3614, 2.3304)	0.8600	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.6800
Yes	37	2 (5.4)	35 (94.6)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	0.4325 (0.0365, 5.1305) 0.5066	0.4951	
No	334	39 (11.7)	295 (88.3)	NE (NE, NE)	159	16 (10.1)	143 (89.9)	NE (NE, NE)	0.8542 (0.4732, 1.5419) 0.6009	0.6012	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.4002
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	1 (14.3)	6 (85.7)	NE (0.7, NE)	0.2887 (0.0181, 4.6154) 0.3797	0.3492	
No	347	40 (11.5)	307 (88.5)	NE (NE, NE)	165	16 (9.7)	149 (90.3)	NE (NE, NE)	0.8565 (0.4752, 1.5437) 0.6062	0.6065	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.5535
Normal Function	201	19 (9.5)	182 (90.5)	NE (NE, NE)	80	7 (8.8)	73 (91.3)	NE (NE, NE)	0.8189 (0.3387, 1.9803) 0.6575	0.6572	
Mild Impairment	123	15 (12.2)	108 (87.8)	NE (NE, NE)	65	7 (10.8)	58 (89.2)	NE (11.3, NE)	0.7902 (0.3171, 1.9692) 0.6133	0.6128	
Moderate Impairment	41	7 (17.1)	34 (82.9)	NE (NE, NE)	23	2 (8.7)	21 (91.3)	NE (NE, NE)	1.8041 (0.3744, 8.6944) 0.4621	0.4556	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.0771
Normal Function	170	20 (11.8)	150 (88.2)	NE (NE, NE)	88	5 (5.7)	83 (94.3)	NE (NE, NE)	1.3612 (0.5032, 3.6822) 0.5436	0.5417	
Mild Impairment	194	21 (10.8)	173 (89.2)	NE (NE, NE)	82	12 (14.6)	70 (85.4)	NE (11.3, NE)	0.5720 (0.2793, 1.1716) 0.1268	0.1222	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.5560
Yes	331	35 (10.6)	296 (89.4)	NE (NE, NE)	146	15 (10.3)	131 (89.7)	NE (NE, NE)	0.7592 (0.4113, 1.4016) 0.3785	0.3776	
No	40	6 (15.0)	34 (85.0)	NE (NE, NE)	26	2 (7.7)	24 (92.3)	NE (NE, NE)	1.4654 (0.2838, 7.5662) 0.6482	0.6462	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.6211
Positive	329	37 (11.2)	292 (88.8)	NE (NE, NE)	152	16 (10.5)	136 (89.5)	NE (NE, NE)	0.7807 (0.4306, 1.4154) 0.4147	0.4144	
Negative	42	4 (9.5)	38 (90.5)	NE (NE, NE)	20	1 (5.0)	19 (95.0)	NE (NE, NE)	1.5626 (0.1699, 14.3740) 0.6934	0.6911	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Stomatitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (derived)											0.1071
Positive	331	37 (11.2)	294 (88.8)	NE (NE, NE)	155	17 (11.0)	138 (89.0)	NE (NE, NE)	0.7459 (0.4163, 1.3362)	0.3233	
Negative	40	4 (10.0)	36 (90.0)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	0.3243 (NE, NE) 0.9960	0.2387	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Gastrointestinal disorders; PT: Abdominal pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.3718
HER2 IHC 1+	214	16 (7.5)	198 (92.5)	NE (NE, NE)	100	5 (5.0)	95 (95.0)	NE (NE, NE)	0.9705 (0.3463, 2.7201) 0.9546	0.9544	
HER2 IHC 2+/ISH Negative	157	19 (12.1)	138 (87.9)	NE (NE, NE)	72	3 (4.2)	69 (95.8)	NE (8.6, NE)	2.5074 (0.7369, 8.5317) 0.1412	0.1281	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.1964
1	220	19 (8.6)	201 (91.4)	NE (NE, NE)	94	6 (6.4)	88 (93.6)	NE (NE, NE)	1.0221 (0.4012, 2.6039) 0.9635	0.9641	
>=2	150	16 (10.7)	134 (89.3)	NE (NE, NE)	78	2 (2.6)	76 (97.4)	NE (7.1, NE)	3.0620 (0.6954, 13.4831) 0.1390	0.1196	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.2190
Yes	233	29 (12.4)	204 (87.6)	NE (NE, NE)	112	7 (6.3)	105 (93.8)	NE (8.6, NE)	1.4042 (0.6047, 3.2604) 0.4296	0.4275	
No	98	4 (4.1)	94 (95.9)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9959	0.2267	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5664
<65	289	28 (9.7)	261 (90.3)	NE (NE, NE)	126	5 (4.0)	121 (96.0)	NE (NE, NE)	1.7458 (0.6645, 4.5866) 0.2582	0.2524	
>=65	82	7 (8.5)	75 (91.5)	NE (NE, NE)	46	3 (6.5)	43 (93.5)	NE (8.2, NE)	1.1202 (0.2858, 4.3913) 0.8706	0.8698	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9998
<75	357	35 (9.8)	322 (90.2)	NE (NE, NE)	163	8 (4.9)	155 (95.1)	NE (NE, NE)	1.4670 (0.6720, 3.2026) 0.3361	0.3329	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.4743
White	175	21 (12.0)	154 (88.0)	NE (NE, NE)	85	6 (7.1)	79 (92.9)	NE (NE, NE)	1.2887 (0.5133, 3.2357) 0.5892	0.5886	
Non-White	196	14 (7.1)	182 (92.9)	NE (NE, NE)	86	2 (2.3)	84 (97.7)	NE (NE, NE)	2.2494 (0.5027, 10.0639) 0.2890	0.2764	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.5232
Asia	147	3 (2.0)	144 (98.0)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (8.6, NE)	0.9579 (0.0963, 9.5293) 0.9707	0.9710	
North America	58	11 (19.0)	47 (81.0)	NE (15.1, NE)	28	1 (3.6)	27 (96.4)	NE (NE, NE)	3.6183 (0.4564, 28.6877) 0.2235	0.1933	
Europe + Israel	166	21 (12.7)	145 (87.3)	NE (NE, NE)	81	6 (7.4)	75 (92.6)	NE (NE, NE)	1.3570 (0.5403, 3.4079) 0.5159	0.5145	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.3660
0	199	16 (8.0)	183 (92.0)	NE (NE, NE)	95	5 (5.3)	90 (94.7)	NE (NE, NE)	1.1537 (0.4164, 3.1963) 0.7833	0.7832	
1	172	19 (11.0)	153 (89.0)	NE (NE, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	2.0996 (0.6093, 7.2348) 0.2400	0.2298	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.0880
0	60	2 (3.3)	58 (96.7)	NE (NE, NE)	31	1 (3.2)	30 (96.8)	NE (NE, NE)	1.0165 (0.0921, 11.2135) 0.9894	0.9893	
1	107	5 (4.7)	102 (95.3)	NE (NE, NE)	48	4 (8.3)	44 (91.7)	NE (NE, NE)	0.4328 (0.1140, 1.6430) 0.2185	0.2061	
2	114	20 (17.5)	94 (82.5)	NE (NE, NE)	50	1 (2.0)	49 (98.0)	NE (NE, NE)	7.1957 (0.9594, 53.9682) 0.0549	0.0249	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	8 (8.9)	82 (91.1)	NE (NE, NE)	43	2 (4.7)	41 (95.3)	NE (8.6, NE)	1.1067 (0.2201, 5.5655) 0.9021	0.9011	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.3555
PD	173	18 (10.4)	155 (89.6)	NE (NE, NE)	77	4 (5.2)	73 (94.8)	NE (NE, NE)	1.5739 (0.5247, 4.7210)	0.4141	
PR	48	3 (6.3)	45 (93.8)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	0.4183 (NE, NE)	0.3042	
SD	82	6 (7.3)	76 (92.7)	NE (NE, NE)	54	4 (7.4)	50 (92.6)	NE (8.6, NE)	0.5453 (0.1466, 2.0275)	0.3596	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.9698
Yes	37	6 (16.2)	31 (83.8)	NE (15.1, NE)	13	1 (7.7)	12 (92.3)	NE (7.1, NE)	1.5856 (0.1823, 13.7917)	0.6735	
No	334	29 (8.7)	305 (91.3)	NE (NE, NE)	159	7 (4.4)	152 (95.6)	NE (NE, NE)	1.4720 (0.6375, 3.3989)	0.3652	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.5356
Yes	24	3 (12.5)	21 (87.5)	NE (NE, NE)	7	1 (14.3)	6 (85.7)	NE (7.1, NE)	0.8198 (0.0841, 7.9915)	0.8642	
No	347	32 (9.2)	315 (90.8)	NE (NE, NE)	165	7 (4.2)	158 (95.8)	NE (NE, NE)	1.6049 (0.7001, 3.6791)	0.2594	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.7136
Normal Function	201	17 (8.5)	184 (91.5)	NE (NE, NE)	80	4 (5.0)	76 (95.0)	NE (8.6, NE)	1.3483 (0.4486, 4.0524) 0.5946	0.5933	
Mild Impairment	123	13 (10.6)	110 (89.4)	NE (NE, NE)	65	2 (3.1)	63 (96.9)	NE (NE, NE)	2.4670 (0.5448, 11.1699) 0.2412	0.2267	
Moderate Impairment	41	5 (12.2)	36 (87.8)	NE (NE, NE)	23	2 (8.7)	21 (91.3)	NE (7.1, NE)	1.2382 (0.2395, 6.4019) 0.7988	0.7984	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1019
Normal Function	170	18 (10.6)	152 (89.4)	NE (NE, NE)	88	2 (2.3)	86 (97.7)	NE (NE, NE)	3.1511 (0.7180, 13.8301) 0.1283	0.1091	
Mild Impairment	194	17 (8.8)	177 (91.2)	NE (NE, NE)	82	6 (7.3)	76 (92.7)	NE (8.2, NE)	0.9450 (0.3678, 2.4277) 0.9064	0.9061	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1525
Yes	331	31 (9.4)	300 (90.6)	NE (NE, NE)	146	8 (5.5)	138 (94.5)	NE (NE, NE)	1.2699 (0.5770, 2.7950) 0.5527	0.5518	
No	40	4 (10.0)	36 (90.0)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9953	0.1235	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.5261
Positive	329	33 (10.0)	296 (90.0)	NE (NE, NE)	152	7 (4.6)	145 (95.4)	NE (NE, NE)	1.6192 (0.7085, 3.7007) 0.2531	0.2487	
Negative	42	2 (4.8)	40 (95.2)	NE (NE, NE)	20	1 (5.0)	19 (95.0)	NE (NE, NE)	0.9488 (0.0860, 10.4650) 0.9658	0.9658	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Gastrointestinal disorders; PT: Abdominal pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.4593
Positive	331	33 (10.0)	298 (90.0)	NE (NE, NE)	155	7 (4.5)	148 (95.5)	NE (NE, NE)	1.6411 (0.7179, 3.7515) 0.2403	0.2356	
Negative	40	2 (5.0)	38 (95.0)	NE (NE, NE)	17	1 (5.9)	16 (94.1)	NE (NE, NE)	0.8182 (0.0741, 9.0303) 0.8699	0.8697	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Dyspepsia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.5352
HER2 IHC 1+	214	15 (7.0)	199 (93.0)	NE (NE, NE)	100	6 (6.0)	94 (94.0)	NE (NE, NE)	0.8779 (0.3350, 2.3009) 0.7911	0.7921	
HER2 IHC 2+/ISH Negative	157	19 (12.1)	138 (87.9)	NE (NE, NE)	72	5 (6.9)	67 (93.1)	NE (NE, NE)	1.3840 (0.5115, 3.7447) 0.5222	0.5203	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Dyspepsia

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting									0.0857
1	220	19 (8.6)	201 (91.4)	94	9 (9.6)	85 (90.4)	NE (NE, NE)	0.7288 (0.3268, 1.6255) 0.4395	0.4380
>=2	150	14 (9.3)	136 (90.7)	78	2 (2.6)	76 (97.4)	NE (NE, NE)	2.6228 (0.5850, 11.7583) 0.2078	0.1912

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Dyspepsia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.7795
Yes	233	25 (10.7)	208 (89.3)	NE (NE, NE)	112	7 (6.3)	105 (93.8)	NE (NE, NE)	1.3842 (0.5935, 3.2280) 0.4517	0.4489	
No	98	9 (9.2)	89 (90.8)	NE (NE, NE)	43	3 (7.0)	40 (93.0)	NE (NE, NE)	0.9286 (0.2464, 3.4993) 0.9129	0.9136	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Dyspepsia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1591
<65	289	30 (10.4)	259 (89.6)	NE (NE, NE)	126	7 (5.6)	119 (94.4)	NE (NE, NE)	1.4902 (0.6485, 3.4243) 0.3473	0.3437	
>=65	82	4 (4.9)	78 (95.1)	NE (NE, NE)	46	4 (8.7)	42 (91.3)	NE (NE, NE)	0.4015 (0.0981, 1.6424) 0.2042	0.1895	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Dyspepsia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											1.0000
<75	357	34 (9.5)	323 (90.5)	NE (NE, NE)	163	11 (6.7)	152 (93.3)	NE (NE, NE)	1.0695 (0.5362, 2.1332) 0.8488	0.8486	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Dyspepsia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.2680
White	175	21 (12.0)	154 (88.0)	NE (NE, NE)	85	5 (5.9)	80 (94.1)	NE (NE, NE)	1.6063 (0.5992, 4.3059) 0.3462	0.3418	
Non-White	196	13 (6.6)	183 (93.4)	NE (NE, NE)	86	6 (7.0)	80 (93.0)	NE (NE, NE)	0.7109 (0.2653, 1.9049) 0.4974	0.4951	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Dyspepsia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.3686
Asia	147	9 (6.1)	138 (93.9)	NE (NE, NE)	63	5 (7.9)	58 (92.1)	NE (NE, NE)	0.5937 (0.1954, 1.8038) 0.3578	0.3531	
North America	58	5 (8.6)	53 (91.4)	NE (NE, NE)	28	1 (3.6)	27 (96.4)	NE (NE, NE)	1.7353 (0.1988, 15.1466) 0.6180	0.6117	
Europe + Israel	166	20 (12.0)	146 (88.0)	NE (NE, NE)	81	5 (6.2)	76 (93.8)	NE (NE, NE)	1.5591 (0.5792, 4.1967) 0.3794	0.3748	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Dyspepsia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.6007
0	199	19 (9.5)	180 (90.5)	NE (NE, NE)	95	7 (7.4)	88 (92.6)	NE (NE, NE)	0.9236 (0.3826, 2.2295) 0.8597	0.8612	
1	172	15 (8.7)	157 (91.3)	NE (NE, NE)	77	4 (5.2)	73 (94.8)	NE (NE, NE)	1.4288 (0.4693, 4.3506) 0.5299	0.5285	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Dyspepsia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1194
0	60	2 (3.3)	58 (96.7)	NE (NE, NE)	31	4 (12.9)	27 (87.1)	NE (NE, NE)	0.1311 (0.0218, 0.7885) 0.0265	0.0109	
1	107	9 (8.4)	98 (91.6)	NE (NE, NE)	48	2 (4.2)	46 (95.8)	NE (NE, NE)	1.8868 (0.4071, 8.7453) 0.4172	0.4091	
2	114	13 (11.4)	101 (88.6)	NE (NE, NE)	50	2 (4.0)	48 (96.0)	NE (NE, NE)	2.0787 (0.4605, 9.3845) 0.3413	0.3312	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Dyspepsia

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 (11.1)	80 (88.9)	NE (NE, NE)	43 (7.0)	40 (93.0)	NE (NE, NE)	1.1836 (0.3176, 4.4104) 0.8017	0.8014	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Dyspepsia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.6417
PD	173	10 (5.8)	163 (94.2)	NE (NE, NE)	77	6 (7.8)	71 (92.2)	NE (NE, NE)	0.5515 (0.1969, 1.5449)	0.2501	
PR	48	5 (10.4)	43 (89.6)	NE (NE, NE)	21	2 (9.5)	19 (90.5)	NE (NE, NE)	0.2575 (0.1200, 3.7894)	0.6527	
SD	82	7 (8.5)	75 (91.5)	NE (NE, NE)	54	3 (5.6)	51 (94.4)	NE (NE, NE)	0.6742 (0.1200, 3.7894)	0.8279	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Dyspepsia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.7169
Yes	37	6 (16.2)	31 (83.8)	NE (NE, NE)	13	2 (15.4)	11 (84.6)	NE (0.9, NE)	0.8634 (0.1721, 4.3308)	0.8582	
No	334	28 (8.4)	306 (91.6)	NE (NE, NE)	159	9 (5.7)	150 (94.3)	NE (NE, NE)	1.1042 (0.5148, 2.3685)	0.7983	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Dyspepsia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.1267
Yes	24	2 (8.3)	22 (91.7)	NE (NE, NE)	7	2 (28.6)	5 (71.4)	NE (0.3, NE)	0.2852 (0.0401, 2.0263) 0.2098	0.1810	
No	347	32 (9.2)	315 (90.8)	NE (NE, NE)	165	9 (5.5)	156 (94.5)	NE (NE, NE)	1.2694 (0.5998, 2.6864) 0.5329	0.5314	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Dyspepsia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.9025
Normal Function	201	21 (10.4)	180 (89.6)	NE (NE, NE)	80	6 (7.5)	74 (92.5)	NE (NE, NE)	1.0582 (0.4218, 2.6549) 0.9041	0.9040	
Mild Impairment	123	9 (7.3)	114 (92.7)	NE (NE, NE)	65	3 (4.6)	62 (95.4)	NE (NE, NE)	1.1592 (0.3039, 4.4216) 0.8288	0.8286	
Moderate Impairment	41	3 (7.3)	38 (92.7)	NE (NE, NE)	23	2 (8.7)	21 (91.3)	NE (NE, NE)	0.6954 (0.1151, 4.2022) 0.6922	0.6907	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Dyspepsia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.5671
Normal Function	170	16 (9.4)	154 (90.6)	NE (NE, NE)	88	7 (8.0)	81 (92.0)	NE (NE, NE)	0.8730 (0.3545, 2.1497) 0.7677	0.7679	
Mild Impairment	194	17 (8.8)	177 (91.2)	NE (NE, NE)	82	4 (4.9)	78 (95.1)	NE (NE, NE)	1.4417 (0.4791, 4.3380) 0.5151	0.5120	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Gastrointestinal disorders; PT: Dyspepsia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.0311
Yes	331	28 (8.5)	303 (91.5)	NE (NE, NE)	146	11 (7.5)	135 (92.5)	NE (NE, NE)	0.8986 (0.4439, 1.8190) 0.7663	0.7660	
No	40	6 (15.0)	34 (85.0)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9953	0.1359	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Dyspepsia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.4431
Positive	329	33 (10.0)	296 (90.0)	NE (NE, NE)	152	10 (6.6)	142 (93.4)	NE (NE, NE)	1.1660 (0.5697, 2.3868) 0.6743	0.6736	
Negative	42	1 (2.4)	41 (97.6)	NE (NE, NE)	20	1 (5.0)	19 (95.0)	NE (NE, NE)	0.4939 (0.0309, 7.8964) 0.6179	0.6106	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Gastrointestinal disorders; PT: Dyspepsia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.0787
Positive	331	34 (10.3)	297 (89.7)	NE (NE, NE)	155	10 (6.5)	145 (93.5)	NE (NE, NE)	1.2328 (0.6039, 2.5166)	0.5642	
Negative	40	0	40 (100)	NE (NE, NE)	17	1 (5.9)	16 (94.1)	NE (NE, NE)	0.0000 (0.0000, ) 0.9978	0.1299	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal pain upper

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.3752
HER2 IHC 1+	214	21 (9.8)	193 (90.2)	NE (NE, NE)	100	7 (7.0)	93 (93.0)	NE (NE, NE)	1.1169 (0.4687, 2.6616) 0.8029	0.8030	
HER2 IHC 2+/ISH Negative	157	10 (6.4)	147 (93.6)	NE (NE, NE)	72	6 (8.3)	66 (91.7)	NE (NE, NE)	0.5927 (0.2120, 1.6567) 0.3186	0.3133	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal pain upper

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.8834
1	220	23 (10.5)	197 (89.5)	NE (NE, NE)	94	9 (9.6)	85 (90.4)	NE (NE, NE)	0.9001 (0.4134, 1.9601)	0.7891	
>=2	150	8 (5.3)	142 (94.7)	NE (NE, NE)	78	4 (5.1)	74 (94.9)	NE (NE, NE)	0.7593 (0.2202, 2.6189)	0.6604	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Abdominal pain upper

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.2090
Yes	233	23 (9.9)	210 (90.1)	NE (NE, NE)	112	7 (6.3)	105 (93.8)	NE (NE, NE)	1.2026 (0.5073, 2.8508) 0.6753	0.6762	
No	98	7 (7.1)	91 (92.9)	NE (NE, NE)	43	5 (11.6)	38 (88.4)	NE (NE, NE)	0.5236 (0.1649, 1.6627) 0.2724	0.2617	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Gastrointestinal disorders; PT: Abdominal pain upper

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4369
<65	289	28 (9.7)	261 (90.3)	NE (NE, NE)	126	10 (7.9)	116 (92.1)	NE (NE, NE)	0.9926 (0.4772, 2.0644) 0.9841	0.9816	
>=65	82	3 (3.7)	79 (96.3)	NE (NE, NE)	46	3 (6.5)	43 (93.5)	NE (NE, NE)	0.3713 (0.0724, 1.9038) 0.2349	0.2178	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal pain upper

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9999
<75	357	31 (8.7)	326 (91.3)	NE (NE, NE)	163	13 (8.0)	150 (92.0)	NE (NE, NE)	0.8440 (0.4365, 1.6318) 0.6141	0.6114	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Gastrointestinal disorders; PT: Abdominal pain upper

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.6107
White	175	9 (5.1)	166 (94.9)	NE (NE, NE)	85	5 (5.9)	80 (94.1)	NE (NE, NE)	0.7075 (0.2331, 2.1472) 0.5413	0.5394	
Non-White	196	22 (11.2)	174 (88.8)	NE (NE, NE)	86	8 (9.3)	78 (90.7)	NE (NE, NE)	0.9564 (0.4210, 2.1727) 0.9152	0.9115	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal pain upper

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.4193
Asia	147	17 (11.6)	130 (88.4)	NE (NE, NE)	63	6 (9.5)	57 (90.5)	NE (NE, NE)	0.9531 (0.3704, 2.4526) 0.9207	0.9119	
North America	58	2 (3.4)	56 (96.6)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9974	0.4443	
Europe + Israel	166	12 (7.2)	154 (92.8)	NE (NE, NE)	81	7 (8.6)	74 (91.4)	NE (NE, NE)	0.6950 (0.2704, 1.7865) 0.4501	0.4471	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal pain upper

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.2167
0	199	20 (10.1)	179 (89.9)	NE (NE, NE)	95	6 (6.3)	89 (93.7)	NE (NE, NE)	1.3799 (0.5500, 3.4621) 0.4927	0.4945	
1	172	11 (6.4)	161 (93.6)	NE (NE, NE)	77	7 (9.1)	70 (90.9)	NE (NE, NE)	0.4638 (0.1739, 1.2373) 0.1249	0.1170	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal pain upper

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.7854
0	60	2 (3.3)	58 (96.7)	NE (NE, NE)	31	2 (6.5)	29 (93.5)	NE (NE, NE)	0.4096 (0.0562, 2.9857)	0.3635	
1	107	7 (6.5)	100 (93.5)	NE (NE, NE)	48	4 (8.3)	44 (91.7)	NE (NE, NE)	0.7446 (0.2177, 2.5462)	0.6355	
2	114	12 (10.5)	102 (89.5)	NE (NE, NE)	50	4 (8.0)	46 (92.0)	NE (NE, NE)	0.6383 (0.3129, 3.1611)	0.9901	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal pain upper

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	10 (11.1)	80 (88.9)	NE (NE, NE)	43	3 (7.0)	40 (93.0)	NE (NE, NE)	1.0845 (0.2887, 4.0734) 0.9044	0.9056	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal pain upper

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.6347
PD	173	13 (7.5)	160 (92.5)	NE (NE, NE)	77	5 (6.5)	72 (93.5)	NE (NE, NE)	1.0427 (0.3706, 2.9336)	0.9385	
PR	48	4 (8.3)	44 (91.7)	NE (NE, NE)	21	1 (4.8)	20 (95.2)	NE (6.7, NE)	0.6982 (0.0725, 6.7220)	0.7550	
SD	82	6 (7.3)	76 (92.7)	NE (NE, NE)	54	6 (11.1)	48 (88.9)	NE (NE, NE)	0.5132 (0.1607, 1.6393)	0.2512	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Gastrointestinal disorders; PT: Abdominal pain upper

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.6728
Yes	37	2 (5.4)	35 (94.6)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (6.7, NE)	0.4837 (0.0407, 5.7466)	0.5573	
No	334	29 (8.7)	305 (91.3)	NE (NE, NE)	159	12 (7.5)	147 (92.5)	NE (NE, NE)	0.9165 (0.4631, 1.8138)	0.7998	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal pain upper

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.6557
Yes	24	2 (8.3)	22 (91.7)	NE (NE, NE)	7	1 (14.3)	6 (85.7)	NE (6.7, NE)	0.3176 (0.0267, 3.7793) 0.3640	0.3404	
No	347	29 (8.4)	318 (91.6)	NE (NE, NE)	165	12 (7.3)	153 (92.7)	NE (NE, NE)	0.9307 (0.4707, 1.8402) 0.8363	0.8340	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Gastrointestinal disorders; PT: Abdominal pain upper

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.3137
Normal Function	201	21 (10.4)	180 (89.6)	NE (NE, NE)	80	5 (6.3)	75 (93.8)	NE (NE, NE)	1.3641 (0.5096, 3.6514) 0.5365	0.5332	
Mild Impairment	123	8 (6.5)	115 (93.5)	NE (NE, NE)	65	7 (10.8)	58 (89.2)	NE (NE, NE)	0.4415 (0.1540, 1.2656) 0.1281	0.1174	
Moderate Impairment	41	2 (4.9)	39 (95.1)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	0.9530 (0.0858, 10.5798) 0.9687	0.9690	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal pain upper

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.4197
Normal Function	170	16 (9.4)	154 (90.6)	NE (NE, NE)	88	9 (10.2)	79 (89.8)	NE (NE, NE)	0.6767 (0.2944, 1.5559) 0.3579	0.3554	
Mild Impairment	194	15 (7.7)	179 (92.3)	NE (NE, NE)	82	4 (4.9)	78 (95.1)	NE (NE, NE)	1.3702 (0.4504, 4.1684) 0.5790	0.5789	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal pain upper

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1913
Yes	331	29 (8.8)	302 (91.2)	NE (NE, NE)	146	13 (8.9)	133 (91.1)	NE (NE, NE)	0.7865 (0.4051, 1.5271) 0.4781	0.4757	
No	40	2 (5.0)	38 (95.0)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9968	0.3098	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal pain upper

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.5501
Positive	329	30 (9.1)	299 (90.9)	NE (NE, NE)	152	12 (7.9)	140 (92.1)	NE (NE, NE)	0.9194 (0.4662, 1.8128)	0.8059	
Negative	42	1 (2.4)	41 (97.6)	NE (NE, NE)	20	1 (5.0)	19 (95.0)	NE (NE, NE)	0.2794 (0.0157, 4.9775)	0.3591	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal pain upper

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.8087
Positive	331	29 (8.8)	302 (91.2)	NE (NE, NE)	155	12 (7.7)	143 (92.3)	NE (NE, NE)	0.8950 (0.4521, 1.7717)	0.7476	
Negative	40	2 (5.0)	38 (95.0)	NE (NE, NE)	17	1 (5.9)	16 (94.1)	NE (NE, NE)	0.7502 (0.0513, 7.3486)	0.6978	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Dry mouth

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.3758
HER2 IHC 1+	214	13 (6.1)	201 (93.9)	NE (NE, NE)	100	6 (6.0)	94 (94.0)	NE (NE, NE)	0.9089 (0.3440, 2.4015) 0.8472	0.8480	
HER2 IHC 2+/ISH Negative	157	13 (8.3)	144 (91.7)	NE (NE, NE)	72	3 (4.2)	69 (95.8)	NE (NE, NE)	1.6069 (0.4527, 5.7044) 0.4631	0.4582	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Dry mouth

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting									0.4659
1	220	15 (6.8)	205 (93.2)	94	6 (6.4)	88 (93.6)	NE (NE, NE)	0.9338 (0.3603, 2.4197)	0.8877
>=2	150	11 (7.3)	139 (92.7)	78	3 (3.8)	75 (96.2)	NE (NE, NE)	1.5120 (0.4151, 5.5069)	0.5280

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Dry mouth

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.3144
Yes	233	15 (6.4)	218 (93.6)	NE (NE, NE)	112	4 (3.6)	108 (96.4)	NE (NE, NE)	1.5471 (0.5106, 4.6874) 0.4404	0.4363	
No	98	7 (7.1)	91 (92.9)	NE (NE, NE)	43	4 (9.3)	39 (90.7)	NE (NE, NE)	0.6376 (0.1841, 2.2088) 0.4778	0.4747	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Dry mouth

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8858
<65	289	21 (7.3)	268 (92.7)	NE (NE, NE)	126	7 (5.6)	119 (94.4)	NE (NE, NE)	1.0596 (0.4461, 2.5167) 0.8957	0.8954	
>=65	82	5 (6.1)	77 (93.9)	NE (NE, NE)	46	2 (4.3)	44 (95.7)	NE (NE, NE)	1.3519 (0.2622, 6.9697) 0.7186	0.7143	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Dry mouth

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											1.0000
<75	357	26 (7.3)	331 (92.7)	NE (NE, NE)	163	9 (5.5)	154 (94.5)	NE (NE, NE)	1.1154 (0.5193, 2.3958) 0.7796	0.7793	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Dry mouth

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.5456
White	175	11 (6.3)	164 (93.7)	NE (NE, NE)	85	3 (3.5)	82 (96.5)	NE (NE, NE)	1.5202 (0.4215, 5.4827) 0.5222	0.5192	
Non-White	196	15 (7.7)	181 (92.3)	NE (NE, NE)	86	6 (7.0)	80 (93.0)	NE (NE, NE)	0.9392 (0.3612, 2.4418) 0.8975	0.8988	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Dry mouth

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.2511
Asia	147	12 (8.2)	135 (91.8)	NE (NE, NE)	63	6 (9.5)	57 (90.5)	NE (NE, NE)	0.7189 (0.2668, 1.9371) 0.5141	0.5142	
North America	58	5 (8.6)	53 (91.4)	NE (NE, NE)	28	2 (7.1)	26 (92.9)	NE (NE, NE)	1.0227 (0.1971, 5.3068) 0.9786	0.9810	
Europe + Israel	166	9 (5.4)	157 (94.6)	NE (NE, NE)	81	1 (1.2)	80 (98.8)	NE (NE, NE)	3.9123 (0.4934, 31.0250) 0.1966	0.1638	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Dry mouth

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.5953
0	199	14 (7.0)	185 (93.0)	NE (NE, NE)	95	4 (4.2)	91 (95.8)	NE (NE, NE)	1.4323 (0.4684, 4.3797) 0.5287	0.5265	
1	172	12 (7.0)	160 (93.0)	NE (NE, NE)	77	5 (6.5)	72 (93.5)	NE (NE, NE)	0.9062 (0.3157, 2.6017) 0.8548	0.8554	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Dry mouth

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.7512
0	60	6 (10.0)	54 (90.0)	NE (NE, NE)	31	3 (9.7)	28 (90.3)	NE (NE, NE)	0.8363 (0.2055, 3.4026)	0.8041	
1	107	8 (7.5)	99 (92.5)	NE (NE, NE)	48	2 (4.2)	46 (95.8)	NE (NE, NE)	1.6193 (0.3415, 7.6777)	0.5406	
2	114	6 (5.3)	108 (94.7)	NE (NE, NE)	50	1 (2.0)	49 (98.0)	NE (NE, NE)	2.3467 (0.2814, 19.5720)	0.4167	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Dry mouth

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 (6.7)	84 (93.3)	NE (NE, NE)	43 (7.0)	40 (93.0)	NE (NE, NE)	0.7580 (0.1859, 3.0903) 0.6992	0.7012	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Dry mouth

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.2603
PD	173	11 (6.4)	162 (93.6)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	4.3794 (0.5631, 34.0608) 0.1582	0.1232	
PR	48	4 (8.3)	44 (91.7)	NE (NE, NE)	21	1 (4.8)	20 (95.2)	NE (NE, NE)	1.5930 (0.1778, 14.2692) 0.6772	0.6745	
SD	82	3 (3.7)	79 (96.3)	NE (NE, NE)	54	3 (5.6)	51 (94.4)	NE (NE, NE)	0.5820 (0.1159, 2.9228) 0.5109	0.5060	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Dry mouth

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.7411
Yes	37	5 (13.5)	32 (86.5)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (6.0, NE)	1.5157 (0.1737, 13.2235)	0.7067	0.7047
No	334	21 (6.3)	313 (93.7)	NE (NE, NE)	159	8 (5.0)	151 (95.0)	NE (NE, NE)	1.0608 (0.4669, 2.4102)	0.8880	0.8873

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Gastrointestinal disorders; PT: Dry mouth

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.8239
Yes	24	3 (12.5)	21 (87.5)	NE (NE, NE)	7	1 (14.3)	6 (85.7)	NE (6.0, NE)	0.7985 (0.0813, 7.8377)	0.8466	
No	347	23 (6.6)	324 (93.4)	NE (NE, NE)	165	8 (4.8)	157 (95.2)	NE (NE, NE)	1.1661 (0.5186, 2.6222)	0.7094	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Dry mouth

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.4089
Normal Function	201	13 (6.5)	188 (93.5)	NE (NE, NE)	80	5 (6.3)	75 (93.8)	NE (NE, NE)	0.9513 (0.3384, 2.6740) 0.9245	0.9246	
Mild Impairment	123	10 (8.1)	113 (91.9)	NE (NE, NE)	65	2 (3.1)	63 (96.9)	NE (NE, NE)	2.0914 (0.4512, 9.6941) 0.3457	0.3355	
Moderate Impairment	41	2 (4.9)	39 (95.1)	NE (NE, NE)	23	2 (8.7)	21 (91.3)	NE (NE, NE)	0.4992 (0.0700, 3.5584) 0.4881	0.4794	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Dry mouth

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.2581
Normal Function	170	13 (7.6)	157 (92.4)	NE (NE, NE)	88	7 (8.0)	81 (92.0)	NE (NE, NE)	0.8746 (0.3477, 2.1997) 0.7759	0.7764	
Mild Impairment	194	12 (6.2)	182 (93.8)	NE (NE, NE)	82	2 (2.4)	80 (97.6)	NE (NE, NE)	1.9335 (0.4271, 8.7526) 0.3921	0.3839	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Gastrointestinal disorders; PT: Dry mouth

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.8725
Yes	331	22 (6.6)	309 (93.4)	NE (NE, NE)	146	7 (4.8)	139 (95.2)	NE (NE, NE)	1.1981 (0.5092, 2.8189) 0.6789	0.6785	
No	40	4 (10.0)	36 (90.0)	NE (NE, NE)	26	2 (7.7)	24 (92.3)	NE (NE, NE)	1.0112 (0.1749, 5.8478) 0.9900	0.9888	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Dry mouth

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.6871
Positive	329	22 (6.7)	307 (93.3)	NE (NE, NE)	152	8 (5.3)	144 (94.7)	NE (NE, NE)	1.0660 (0.4712, 2.4113) 0.8781	0.8779	
Negative	42	4 (9.5)	38 (90.5)	NE (NE, NE)	20	1 (5.0)	19 (95.0)	NE (NE, NE)	1.8635 (0.2082, 16.6801) 0.5778	0.5717	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Gastrointestinal disorders; PT: Dry mouth

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.8004
Positive	331	22 (6.6)	309 (93.4)	NE (NE, NE)	155	8 (5.2)	147 (94.8)	NE (NE, NE)	1.0841 (0.4793, 2.4524) 0.8462	0.8460	
Negative	40	4 (10.0)	36 (90.0)	NE (NE, NE)	17	1 (5.9)	16 (94.1)	NE (NE, NE)	1.5989 (0.1783, 14.3405) 0.6750	0.6722	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Gastrointestinal disorders; PT: Gastroesophageal reflux disease

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.6282
HER2 IHC 1+	214	11 (5.1)	203 (94.9)	NE (NE, NE)	100	1 (1.0)	99 (99.0)	NE (NE, NE)	4.5034 (0.5781, 35.0834) 0.1508	0.1153	
HER2 IHC 2+/ISH Negative	157	12 (7.6)	145 (92.4)	NE (NE, NE)	72	2 (2.8)	70 (97.2)	NE (NE, NE)	2.0738 (0.4570, 9.4105) 0.3445	0.3347	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Gastrooesophageal reflux disease

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.7942
1	220	10 (4.5)	210 (95.5)	NE (NE, NE)	94	1 (1.1)	93 (98.9)	NE (NE, NE)	3.4488 (0.4376, 27.1827) 0.2399	0.2110	
>=2	150	12 (8.0)	138 (92.0)	NE (NE, NE)	78	2 (2.6)	76 (97.4)	NE (NE, NE)	2.5521 (0.5619, 11.5903) 0.2249	0.2090	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Gastroesophageal reflux disease

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.2169
Yes	233	16 (6.9)	217 (93.1)	NE (NE, NE)	112	1 (0.9)	111 (99.1)	NE (NE, NE)	5.9832 (0.7853, 45.5859) 0.0842	0.0498	
No	98	7 (7.1)	91 (92.9)	NE (NE, NE)	43	2 (4.7)	41 (95.3)	NE (NE, NE)	1.3586 (0.2808, 6.5745) 0.7032	0.7021	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.8.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Gastrointestinal disorders; PT: Gastroesophageal reflux disease

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8681
<65	289	18 (6.2)	271 (93.8)	NE (NE, NE)	126	2 (1.6)	124 (98.4)	NE (NE, NE)	3.0347 (0.6970, 13.2126) 0.1391	0.1201	
>=65	82	5 (6.1)	77 (93.9)	NE (NE, NE)	46	1 (2.2)	45 (97.8)	NE (NE, NE)	2.6086 (0.3031, 22.4533) 0.3827	0.3647	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Gastrointestinal disorders; PT: Gastroesophageal reflux disease

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5136
<75	357	22 (6.2)	335 (93.8)	NE (NE, NE)	163	3 (1.8)	160 (98.2)	NE (NE, NE)	2.6460 (0.7848, 8.9213) 0.1166	0.1031	
>=75	14	1 (7.1)	13 (92.9)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9985	0.4227	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Gastroesophageal reflux disease

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.5907
White	175	11 (6.3)	164 (93.7)	NE (NE, NE)	85	1 (1.2)	84 (98.8)	NE (NE, NE)	4.0618 (0.5171, 31.9032) 0.1826	0.1494	
Non-White	196	12 (6.1)	184 (93.9)	NE (NE, NE)	86	2 (2.3)	84 (97.7)	NE (NE, NE)	2.2530 (0.5005, 10.1419) 0.2900	0.2774	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Gastroesophageal reflux disease

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.1095
Asia	147	4 (2.7)	143 (97.3)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (NE, NE)	1.3073 (0.1428, 11.9717) 0.8126	0.8120	
North America	58	7 (12.1)	51 (87.9)	NE (NE, NE)	28	2 (7.1)	26 (92.9)	NE (NE, NE)	0.9445 (0.1855, 4.8088) 0.9452	0.9451	
Europe + Israel	166	12 (7.2)	154 (92.8)	NE (NE, NE)	81	0	81 (100)	NE (NE, NE)	NE (NE, NE) 0.9924	0.0187	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Gastroesophageal reflux disease

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.2842
0	199	15 (7.5)	184 (92.5)	NE (NE, NE)	95	1 (1.1)	94 (98.9)	NE (NE, NE)	6.1807 (0.8123, 47.0304) 0.0786	0.0445	
1	172	8 (4.7)	164 (95.3)	NE (NE, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	1.2938 (0.2674, 6.2588) 0.7488	0.7481	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Gastroesophageal reflux disease

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1624
0	60	4 (6.7)	56 (93.3)	NE (NE, NE)	31	1 (3.2)	30 (96.8)	NE (NE, NE)	1.8316 (0.2039, 16.4558) 0.5890	0.5834	
1	107	5 (4.7)	102 (95.3)	NE (NE, NE)	48	0	48 (100)	NE (NE, NE)	NE (NE, NE) 0.9955	0.1926	
2	114	9 (7.9)	105 (92.1)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	NE (NE, NE) 0.9940	0.0741	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Gastrooesophageal reflux disease

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	5 (5.6)	85 (94.4)	NE (NE, NE)	43	2 (4.7)	41 (95.3)	NE (NE, NE)	0.9541 (0.1799, 5.0605) 0.9560	0.9564	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.8.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Gastrointestinal disorders; PT: Gastroesophageal reflux disease

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.6949
PD	173	14 (8.1)	159 (91.9)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	5.1876 (0.6774, 39.7265)	0.0772	
PR	48	1 (2.1)	47 (97.9)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	NE (NE, NE)	0.5553	
SD	82	3 (3.7)	79 (96.3)	NE (NE, NE)	54	1 (1.9)	53 (98.1)	NE (NE, NE)	1.1893 (0.1170, 12.0868)	0.8834	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Gastroesophageal reflux disease

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.2873
Yes	37	3 (8.1)	34 (91.9)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	0.5131 (0.0510, 5.1611)	0.5644	
No	334	20 (6.0)	314 (94.0)	NE (NE, NE)	159	2 (1.3)	157 (98.7)	NE (NE, NE)	4.0320 (0.9362, 17.3660)	0.0430	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Gastrointestinal disorders; PT: Gastroesophageal reflux disease

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0985
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	1 (14.3)	6 (85.7)	NE (1.4, NE)	0.2212 (0.0132, 3.7032) 0.2940	0.2526	
No	347	22 (6.3)	325 (93.7)	NE (NE, NE)	165	2 (1.2)	163 (98.8)	NE (NE, NE)	4.3289 (1.0118, 18.5212) 0.0482	0.0312	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Gastroesophageal reflux disease

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.4519
Normal Function	201	16 (8.0)	185 (92.0)	NE (NE, NE)	80	1 (1.3)	79 (98.8)	NE (NE, NE)	4.8441 (0.6365, 36.8641) 0.1276	0.0922	
Mild Impairment	123	6 (4.9)	117 (95.1)	NE (NE, NE)	65	2 (3.1)	63 (96.9)	NE (NE, NE)	1.3227 (0.2594, 6.7433) 0.7365	0.7374	
Moderate Impairment	41	1 (2.4)	40 (97.6)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9977	0.4639	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Gastroesophageal reflux disease

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.8782
Normal Function	170	13 (7.6)	157 (92.4)	NE (NE, NE)	88	2 (2.3)	86 (97.7)	NE (NE, NE)	2.8692 (0.6429, 12.8053) 0.1673	0.1486	
Mild Impairment	194	10 (5.2)	184 (94.8)	NE (NE, NE)	82	1 (1.2)	81 (98.8)	NE (NE, NE)	3.2160 (0.4045, 25.5692) 0.2695	0.2433	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Gastrointestinal disorders; PT: Gastroesophageal reflux disease

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.3344
Yes	331	21 (6.3)	310 (93.7)	NE (NE, NE)	146	2 (1.4)	144 (98.6)	NE (NE, NE)	3.8284 (0.8919, 16.4327) 0.0709	0.0521	
No	40	2 (5.0)	38 (95.0)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	0.9433 (0.0839, 10.5998) 0.9623	0.9623	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.9998
Positive	329	23 (7.0)	306 (93.0)	NE (NE, NE)	152	3 (2.0)	149 (98.0)	NE (NE, NE)	2.8905 (0.8620, 9.6925)	0.0720	
Negative	42	0	42 (100)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) NE		

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 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Gastrointestinal disorders; PT: Gastroesophageal reflux disease

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.9998
Positive	331	23 (6.9)	308 (93.1)	NE (NE, NE)	155	3 (1.9)	152 (98.1)	NE (NE, NE)	2.9348 (0.8751, 9.8421)	0.0677	
Negative	40	0	40 (100)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Gastrointestinal disorders; PT: Abdominal distension

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.2057
HER2 IHC 1+	214	10 (4.7)	204 (95.3)	NE (NE, NE)	100	4 (4.0)	96 (96.0)	NE (NE, NE)	1.0329 (0.3224, 3.3092) 0.9566	0.9568	
HER2 IHC 2+/ISH Negative	157	10 (6.4)	147 (93.6)	NE (NE, NE)	72	1 (1.4)	71 (98.6)	NE (NE, NE)	4.4702 (0.5721, 34.9261) 0.1534	0.1177	

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.4350
1	220	12 (5.5)	208 (94.5)	NE (NE, NE)	94	2 (2.1)	92 (97.9)	NE (NE, NE)	2.3922 (0.5346, 10.7043) 0.2539	0.2392	
>=2	150	7 (4.7)	143 (95.3)	NE (NE, NE)	78	3 (3.8)	75 (96.2)	NE (NE, NE)	1.1022 (0.2836, 4.2838) 0.8883	0.8890	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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DE.T.4.8.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Gastrointestinal disorders; PT: Abdominal distension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.1570
Yes	233	9 (3.9)	224 (96.1)	NE (NE, NE)	112	4 (3.6)	108 (96.4)	NE (NE, NE)	1.0300 (0.3168, 3.3495) 0.9608	0.9623	
No	98	11 (11.2)	87 (88.8)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	4.6381 (0.5981, 35.9665) 0.1421	0.1062	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal distension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0405
<65	289	18 (6.2)	271 (93.8)	NE (NE, NE)	126	2 (1.6)	124 (98.4)	NE (NE, NE)	3.7456 (0.8684, 16.1549) 0.0766	0.0572	
>=65	82	2 (2.4)	80 (97.6)	NE (NE, NE)	46	3 (6.5)	43 (93.5)	NE (NE, NE)	0.3263 (0.0541, 1.9677) 0.2219	0.1988	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Abdominal distension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0977
<75	357	20 (5.6)	337 (94.4)	NE (NE, NE)	163	4 (2.5)	159 (97.5)	NE (NE, NE)	2.1101 (0.7199, 6.1848)	0.1639	
>=75	14	0	14 (100)	NE (NE, NE)	9	1 (11.1)	8 (88.9)	NE (1.9, NE)	0.0000 (0.0000, )	0.2294	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal distension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.4625
White	175	8 (4.6)	167 (95.4)	NE (NE, NE)	85	3 (3.5)	82 (96.5)	NE (NE, NE)	1.2262 (0.3248, 4.6291) 0.7635	0.7652	
Non-White	196	12 (6.1)	184 (93.9)	NE (NE, NE)	86	2 (2.3)	84 (97.7)	NE (NE, NE)	2.4467 (0.5464, 10.9565) 0.2421	0.2269	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal distension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.9949
Asia	147	9 (6.1)	138 (93.9)	NE (NE, NE)	63	2 (3.2)	61 (96.8)	NE (NE, NE)	1.7301 (0.3723, 8.0406) 0.4843	0.4793	
North America	58	4 (6.9)	54 (93.1)	NE (NE, NE)	28	1 (3.6)	27 (96.4)	NE (NE, NE)	1.7550 (0.1958, 15.7304) 0.6152	0.6105	
Europe + Israel	166	7 (4.2)	159 (95.8)	NE (NE, NE)	81	2 (2.5)	79 (97.5)	NE (NE, NE)	1.6741 (0.3477, 8.0608) 0.5205	0.5170	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal distension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.0028
0	199	13 (6.5)	186 (93.5)	NE (NE, NE)	95	0	95 (100)	NE (NE, NE)	NE (NE, NE) 0.9922	0.0184	
1	172	7 (4.1)	165 (95.9)	NE (NE, NE)	77	5 (6.5)	72 (93.5)	NE (NE, NE)	0.6024 (0.1910, 1.9003) 0.3872	0.3818	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1858
0	60	3 (5.0)	57 (95.0)	NE (NE, NE)	31	1 (3.2)	30 (96.8)	NE (NE, NE)	1.4053 (0.1460, 13.5258) 0.7684	0.7672	
1	107	8 (7.5)	99 (92.5)	NE (NE, NE)	48	0	48 (100)	NE (NE, NE)	NE (NE, NE) 0.9937	0.0544	
2	114	7 (6.1)	107 (93.9)	NE (NE, NE)	50	3 (6.0)	47 (94.0)	NE (NE, NE)	0.8376 (0.2144, 3.2717) 0.7987	0.7973	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	2 (2.2)	88 (97.8)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	0.9171 (0.0831, 10.1255) 0.9437	0.9436	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Best Response to last prior cancer systemic therapy											0.2000
PD	173	9 (5.2)	164 (94.8)	NE (NE, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	1.8754 (0.4047, 8.6914)	0.4142	
PR	48	1 (2.1)	47 (97.9)	NE (NE, NE)	21	2 (9.5)	19 (90.5)	NE (NE, NE)	0.2052 (0.0186, 2.2698)	0.1528	
SD	82	4 (4.9)	78 (95.1)	NE (NE, NE)	54	1 (1.9)	53 (98.1)	NE (NE, NE)	2.3670 (0.2628, 21.3174)	0.4284	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.3999
Yes	37	2 (5.4)	35 (94.6)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9971	0.3970	
No	334	18 (5.4)	316 (94.6)	NE (NE, NE)	159	5 (3.1)	154 (96.9)	NE (NE, NE)	1.5765 (0.5843, 4.2536) 0.3687	0.3646	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Abdominal distension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.5725
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.5727	
No	347	19 (5.5)	328 (94.5)	NE (NE, NE)	165	5 (3.0)	160 (97.0)	NE (NE, NE)	1.6668 (0.6211, 4.4728) 0.3104	0.3056	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal distension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.6029
Normal Function	201	12 (6.0)	189 (94.0)	NE (NE, NE)	80	2 (2.5)	78 (97.5)	NE (NE, NE)	2.3620 (0.5286, 10.5548) 0.2605	0.2461	
Mild Impairment	123	7 (5.7)	116 (94.3)	NE (NE, NE)	65	3 (4.6)	62 (95.4)	NE (NE, NE)	1.0134 (0.2598, 3.9524) 0.9847	0.9857	
Moderate Impairment	41	1 (2.4)	40 (97.6)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9977	0.4539	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal distension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.2728
Normal Function	170	8 (4.7)	162 (95.3)	NE (NE, NE)	88	1 (1.1)	87 (98.9)	NE (NE, NE)	4.0088 (0.5007, 32.0948) 0.1908	0.1570	
Mild Impairment	194	12 (6.2)	182 (93.8)	NE (NE, NE)	82	4 (4.9)	78 (95.1)	NE (NE, NE)	1.1171 (0.3590, 3.4765) 0.8484	0.8505	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal distension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.4370
Yes	331	19 (5.7)	312 (94.3)	NE (NE, NE)	146	5 (3.4)	141 (96.6)	NE (NE, NE)	1.5855 (0.5913, 4.2515) 0.3597	0.3560	
No	40	1 (2.5)	39 (97.5)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.5751	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal distension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.9998
Positive	329	20 (6.1)	309 (93.9)	NE (NE, NE)	152	5 (3.3)	147 (96.7)	NE (NE, NE)	1.7090 (0.6404, 4.5610)	0.2792	
Negative	42	0	42 (100)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Abdominal distension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.9998
Positive	331	20 (6.0)	311 (94.0)	NE (NE, NE)	155	5 (3.2)	150 (96.8)	NE (NE, NE)	1.7379 (0.6512, 4.6378)	0.2641	
Negative	40	0	40 (100)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Gastritis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.2530
HER2 IHC 1+	214	5 (2.3)	209 (97.7)	NE (NE, NE)	100	0	100 (100)	NE (NE, NE)	NE (NE, NE) 0.9953	0.1612	
HER2 IHC 2+/ISH Negative	157	5 (3.2)	152 (96.8)	NE (NE, NE)	72	1 (1.4)	71 (98.6)	NE (NE, NE)	2.0106 (0.2340, 17.2788) 0.5245	0.5161	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Gastrointestinal disorders; PT: Gastritis

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting									0.6352
1	220	9 (4.1)	211 (95.9) NE (NE, NE)	94	1 (1.1)	93 (98.9) NE (NE, NE)	3.3944 (0.4285, 26.8910) 0.2471	0.2186	
>=2	150	1 (0.7)	149 (99.3) NE (NE, NE)	78	0	78 (100) NE (NE, NE)	NE (NE, NE) 0.9978	0.5122	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.1769
Yes	233	5 (2.1)	228 (97.9)	NE (NE, NE)	112	0	112 (100)	NE (NE, NE)	NE (NE, NE) 0.9951	0.1367	
No	98	3 (3.1)	95 (96.9)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	0.9902 (0.1020, 9.6162) 0.9932	0.9932	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Gastrointestinal disorders; PT: Gastritis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1808
<65	289	7 (2.4)	282 (97.6)	NE (NE, NE)	126	0	126 (100)	NE (NE, NE)	NE (NE, NE) 0.9944	0.0997	
>=65	82	3 (3.7)	79 (96.3)	NE (NE, NE)	46	1 (2.2)	45 (97.8)	NE (NE, NE)	1.4463 (0.1484, 14.0964) 0.7508	0.7510	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Gastritis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9998
<75	357	10 (2.8)	347 (97.2)	NE (NE, NE)	163	1 (0.6)	162 (99.4)	NE (NE, NE)	3.8800 (0.4939, 30.4807)	0.1648	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Gastritis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.2422
White	175	5 (2.9)	170 (97.1)	NE (NE, NE)	85	0	85 (100)	NE (NE, NE)	NE (NE, NE) 0.9953	0.1579	
Non-White	196	5 (2.6)	191 (97.4)	NE (NE, NE)	86	1 (1.2)	85 (98.8)	NE (NE, NE)	1.9412 (0.2259, 16.6813) 0.5456	0.5386	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Gastritis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.3940
Asia	147	4 (2.7)	143 (97.3)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (NE, NE)	1.4365 (0.1595, 12.9356) 0.7467	0.7452	
North America	58	0	58 (100)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) NE		
Europe + Israel	166	6 (3.6)	160 (96.4)	NE (NE, NE)	81	0	81 (100)	NE (NE, NE)	NE (NE, NE) 0.9948	0.1101	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Gastritis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											
0	199	3 (1.5)	196 (98.5)	NE (NE, NE)	95	0	95 (100)	NE (NE, NE)	NE (NE, NE) 0.9962	0.2501	0.4119
1	172	7 (4.1)	165 (95.9)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	2.6319 (0.3207, 21.6001) 0.3676	0.3494	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Gastritis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.3916
0	60	4 (6.7)	56 (93.3)	NE (NE, NE)	31	0	31 (100)	NE (NE, NE)	NE (NE, NE) 0.9957	0.1881	
1	107	2 (1.9)	105 (98.1)	NE (NE, NE)	48	0	48 (100)	NE (NE, NE)	NE (NE, NE) 0.9969	0.3516	
2	114	2 (1.8)	112 (98.2)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	NE (NE, NE) 0.9971	0.3949	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Gastritis

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 (2.2)	88 (97.8)	NE (NE, NE)	43 (2.3)	42 (97.7)	NE (NE, NE)	0.8092 (0.0730, 8.9636) 0.8630	0.8628	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Gastritis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.4216
PD	173	7 (4.0)	166 (96.0)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE) 0.9942	0.0799	
PR	48	0	48 (100)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	NE (NE, NE) NE		
SD	82	3 (3.7)	79 (96.3)	NE (NE, NE)	54	1 (1.9)	53 (98.1)	NE (NE, NE)	1.3120 (0.1327, 12.9701) 0.8163	0.8158	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Gastrointestinal disorders; PT: Gastritis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.7002
Yes	37	1 (2.7)	36 (97.3)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.5533	
No	334	9 (2.7)	325 (97.3)	NE (NE, NE)	159	1 (0.6)	158 (99.4)	NE (NE, NE)	3.6084 (0.4548, 28.6292) 0.2246	0.1940	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Gastritis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.9998
Yes	24	0	24 (100)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE)		
No	347	10 (2.9)	337 (97.1)	NE (NE, NE)	165	1 (0.6)	164 (99.4)	NE (NE, NE)	4.0487 (0.5155, 31.7947) 0.1836	0.1500	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Gastritis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.4732
Normal Function	201	5 (2.5)	196 (97.5)	NE (NE, NE)	80	0	80 (100)	NE (NE, NE)	NE (NE, NE) 0.9954	0.1842	
Mild Impairment	123	4 (3.3)	119 (96.7)	NE (NE, NE)	65	1 (1.5)	64 (98.5)	NE (NE, NE)	1.6202 (0.1772, 14.8150) 0.6691	0.6662	
Moderate Impairment	41	1 (2.4)	40 (97.6)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9977	0.4539	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Gastrointestinal disorders; PT: Gastritis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1657
Normal Function	170	3 (1.8)	167 (98.2)	NE (NE, NE)	88	1 (1.1)	87 (98.9)	NE (NE, NE)	1.2152 (0.1232, 11.9851) 0.8675	0.8672	
Mild Impairment	194	7 (3.6)	187 (96.4)	NE (NE, NE)	82	0	82 (100)	NE (NE, NE)	NE (NE, NE) 0.9945	0.1069	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.8.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Gastrointestinal disorders; PT: Gastritis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.6152
Yes	331	9 (2.7)	322 (97.3)	NE (NE, NE)	146	1 (0.7)	145 (99.3)	NE (NE, NE)	3.6451 (0.4610, 28.8181) 0.2202	0.1893	
No	40	1 (2.5)	39 (97.5)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9984	0.7963	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Gastritis

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.4961
Positive	329	8 (2.4)	321 (97.6)	NE (NE, NE)	152	1 (0.7)	151 (99.3)	NE (NE, NE)	3.0177 (0.3749, 24.2898) 0.2993	0.2753	
Negative	42	2 (4.8)	40 (95.2)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) 0.9968	0.3262	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.5268
Positive	331	8 (2.4)	323 (97.6)	NE (NE, NE)	155	1 (0.6)	154 (99.4)	NE (NE, NE)	3.0742 (0.3819, 24.7436)	0.2665	
Negative	40	2 (5.0)	38 (95.0)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	0.2912 (NE, NE) 0.9969	0.3535	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.6573
HER2 IHC 1+	214	144 (67.3)	70 (32.7)	2.8 (1.8, 4.1)	100	67 (67.0)	33 (33.0)	0.5 (0.5, 1.4)	0.6962 (0.5193, 0.9333) 0.0155	0.0154	
HER2 IHC 2+/ISH Negative	157	107 (68.2)	50 (31.8)	3.4 (2.1, 4.2)	72	47 (65.3)	25 (34.7)	0.7 (0.5, 3.5)	0.7575 (0.5351, 1.0722) 0.1172	0.1226	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.5026
1	220	143 (65.0)	77 (35.0)	3.4 (2.3, 4.2)	94	57 (60.6)	37 (39.4)	0.9 (0.5, 3.9)	0.7949 (0.5833, 1.0835) 0.1464	0.1537	
>=2	150	108 (72.0)	42 (28.0)	2.7 (1.4, 3.5)	78	57 (73.1)	21 (26.9)	0.5 (0.4, 0.9)	0.6627 (0.4783, 0.9183) 0.0134	0.0130	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Prior CDK4/6											
Yes	233	147 (63.1)	86 (36.9)	3.7 (2.7, 4.2)	112	70 (62.5)	42 (37.5)	0.9 (0.5, 3.3)	0.7093 (0.5315, 0.9467) 0.0197	0.0199	0.6851
No	98	75 (76.5)	23 (23.5)	1.4 (0.6, 3.5)	43	32 (74.4)	11 (25.6)	0.5 (0.3, 0.7)	0.7704 (0.5080, 1.1682) 0.2194	0.2261	

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Age											0.9300
<65	289	194 (67.1)	95 (32.9)	2.8 (2.1, 4.1)	126	80 (63.5)	46 (36.5)	0.7 (0.5, 2.1)	0.7433 (0.5711, 0.9675) 0.0274	0.0294	
>=65	82	57 (69.5)	25 (30.5)	3.4 (1.2, 5.4)	46	34 (73.9)	12 (26.1)	0.7 (0.3, 3.5)	0.7044 (0.4592, 1.0807) 0.1086	0.1125	

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Age											0.7820
<75	357	240 (67.2)	117 (32.8)	2.8 (2.1, 4.1)	163	107 (65.6)	56 (34.4)	0.7 (0.5, 1.4)	0.7348 (0.5837, 0.9251) 0.0087	0.0093	
>=75	14	11 (78.6)	3 (21.4)	3.0 (0.7, 4.2)	9	7 (77.8)	2 (22.2)	0.7 (0.2, NE)	0.4613 (0.1657, 1.2844) 0.1386	0.1293	

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Race											0.1095
White	175	110 (62.9)	65 (37.1)	4.2 (3.0, 6.2)	85	46 (54.1)	39 (45.9)	3.5 (0.7, 7.2)	0.8313 (0.5862, 1.1788) 0.2998	0.3301	
Non-White	196	141 (71.9)	55 (28.1)	1.4 (0.7, 2.8)	86	68 (79.1)	18 (20.9)	0.5 (0.3, 0.5)	0.6054 (0.4518, 0.8112) 0.0008	0.0006	

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Region											0.0048
Asia	147	114 (77.6)	33 (22.4)	1.3 (0.5, 2.2)	63	56 (88.9)	7 (11.1)	0.3 (0.3, 0.5)	0.4590 (0.3302, 0.6380) <0.0001	<0.0001	
North America	58	38 (65.5)	20 (34.5)	4.0 (2.1, 5.5)	28	19 (67.9)	9 (32.1)	0.7 (0.3, 3.9)	0.6442 (0.3699, 1.1219) 0.1203	0.1311	
Europe + Israel	166	99 (59.6)	67 (40.4)	4.2 (3.3, 6.4)	81	39 (48.1)	42 (51.9)	5.5 (2.1, 7.2)	0.9762 (0.6703, 1.4216) 0.9000	0.9212	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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DE.T.4.8.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											
0	199	138 (69.3)	61 (30.7)	3.5 (1.4, 4.2)	95	58 (61.1)	37 (38.9)	0.9 (0.5, 3.9)	0.8433 (0.6191, 1.1489) 0.2801	0.3016	0.1551
1	172	113 (65.7)	59 (34.3)	2.8 (2.1, 3.5)	77	56 (72.7)	21 (27.3)	0.5 (0.5, 0.9)	0.5914 (0.4266, 0.8200) 0.0016	0.0015	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.2800
0	60	39 (65.0)	21 (35.0)	2.8 (2.0, 6.3)	31	23 (74.2)	8 (25.8)	0.7 (0.3, 2.1)	0.5121 (0.2998, 0.8748) 0.0143	0.0129	
1	107	71 (66.4)	36 (33.6)	3.7 (1.5, 4.8)	48	31 (64.6)	17 (35.4)	0.7 (0.3, 6.9)	0.7769 (0.5084, 1.1874) 0.2435	0.2421	
2	114	79 (69.3)	35 (30.7)	2.1 (0.7, 3.5)	50	29 (58.0)	21 (42.0)	0.9 (0.5, NE)	0.9982 (0.6501, 1.5329) 0.9936	0.9843	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 (68.9)	28 (31.1)	3.5 (2.1, 5.6)	43 (72.1)	12 (27.9)	0.5 (0.3, 1.4)	0.5617 (0.3601, 0.8759) 0.0110	0.0108	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.4930
PD	173	112 (64.7)	61 (35.3)	3.3 (2.3, 4.3)	77	50 (64.9)	27 (35.1)	0.9 (0.5, 3.5)	0.7026 (0.5018, 0.9840) 0.0400	0.0394	
PR	48	33 (68.8)	15 (31.3)	4.1 (1.4, 9.0)	21	15 (71.4)	6 (28.6)	0.3 (0.3, 2.2)	0.5353 (0.2864, 1.0005) 0.0502	0.0538	
SD	82	57 (69.5)	25 (30.5)	2.2 (0.7, 4.3)	54	35 (64.8)	19 (35.2)	0.6 (0.4, 3.3)	0.8722 (0.5704, 1.3336) 0.5279	0.5359	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Reported history of CNS metastases											0.1922
Yes	37	23 (62.2)	14 (37.8)	2.8 (0.7, NE)	13	10 (76.9)	3 (23.1)	0.4 (0.3, 1.4)	0.5257 (0.2441, 1.1322)	0.1048	
No	334	228 (68.3)	106 (31.7)	3.0 (2.2, 4.1)	159	104 (65.4)	55 (34.6)	0.7 (0.5, 1.8)	0.7473 (0.5912, 0.9447)	0.0156	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.4650
Yes	24	15 (62.5)	9 (37.5)	1.4 (0.3, NE)	7	6 (85.7)	1 (14.3)	1.0 (0.3, 3.9)	0.5768 (0.2166, 1.5365) 0.2710	0.2447	
No	347	236 (68.0)	111 (32.0)	3.0 (2.2, 4.1)	165	108 (65.5)	57 (34.5)	0.7 (0.5, 1.4)	0.7335 (0.5826, 0.9233) 0.0083	0.0093	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.4435
Normal Function	201	140 (69.7)	61 (30.3)	2.8 (1.4, 4.1)	80	48 (60.0)	32 (40.0)	0.9 (0.5, 6.9)	0.8645 (0.6211, 1.2032) 0.3879	0.4136	
Mild Impairment	123	79 (64.2)	44 (35.8)	3.4 (1.8, 4.9)	65	44 (67.7)	21 (32.3)	0.5 (0.5, 1.2)	0.6688 (0.4603, 0.9719) 0.0349	0.0385	
Moderate Impairment	41	29 (70.7)	12 (29.3)	3.5 (0.7, 6.3)	23	18 (78.3)	5 (21.7)	0.7 (0.2, 5.3)	0.5983 (0.3279, 1.0917) 0.0941	0.0943	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.3549
Normal Function	170	111 (65.3)	59 (34.7)	4.2 (2.8, 6.2)	88	59 (67.0)	29 (33.0)	0.7 (0.5, 1.8)	0.6453 (0.4682, 0.8894) 0.0075	0.0070	
Mild Impairment	194	135 (69.6)	59 (30.4)	2.7 (1.4, 3.4)	82	53 (64.6)	29 (35.4)	0.7 (0.4, 2.7)	0.8146 (0.5913, 1.1224) 0.2099	0.2333	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.3057
Yes	331	226 (68.3)	105 (31.7)	3.0 (2.2, 4.0)	146	96 (65.8)	50 (34.2)	0.7 (0.5, 1.8)	0.7516 (0.5906, 0.9566) 0.0203	0.0232	
No	40	25 (62.5)	15 (37.5)	2.2 (0.7, 19.4)	26	18 (69.2)	8 (30.8)	0.5 (0.3, 3.3)	0.5806 (0.3098, 1.0882) 0.0898	0.0750	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.6202
Positive	329	222 (67.5)	107 (32.5)	3.0 (2.1, 4.1)	152	102 (67.1)	50 (32.9)	0.5 (0.5, 1.0)	0.7139 (0.5635, 0.9046) 0.0053	0.0057	
Negative	42	29 (69.0)	13 (31.0)	2.8 (1.6, 6.2)	20	12 (60.0)	8 (40.0)	1.3 (0.5, NE)	0.7427 (0.3676, 1.5006) 0.4072	0.3973	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.6819
Positive	331	223 (67.4)	108 (32.6)	3.0 (2.1, 4.2)	155	102 (65.8)	53 (34.2)	0.7 (0.5, 1.8)	0.7354 (0.5804, 0.9319)	0.0116	
Negative	40	28 (70.0)	12 (30.0)	2.7 (1.6, 4.2)	17	12 (70.6)	5 (29.4)	0.9 (0.3, NE)	0.5261 (0.2561, 1.0807)	0.0763	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0975
HER2 IHC 1+	214	49 (22.9)	165 (77.1)	NE (NE, NE)	100	28 (28.0)	72 (72.0)	NE (6.9, NE)	0.6099 (0.3802, 0.9785) 0.0403	0.0386	
HER2 IHC 2+/ISH Negative	157	43 (27.4)	114 (72.6)	NE (NE, NE)	72	14 (19.4)	58 (80.6)	NE (13.6, NE)	1.0698 (0.5803, 1.9719) 0.8289	0.8307	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.8447
1	220	60 (27.3)	160 (72.7)	NE (NE, NE)	94	25 (26.6)	69 (73.4)	NE (NE, NE)	0.7978 (0.4971, 1.2806) 0.3495	0.3501	
>=2	150	32 (21.3)	118 (78.7)	NE (NE, NE)	78	17 (21.8)	61 (78.2)	NE (13.6, NE)	0.6920 (0.3800, 1.2600) 0.2286	0.2253	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.0047
Yes	233	44 (18.9)	189 (81.1)	NE (NE, NE)	112	29 (25.9)	83 (74.1)	NE (6.9, NE)	0.5127 (0.3164, 0.8307) 0.0067	0.0058	
No	98	37 (37.8)	61 (62.2)	NE (9.7, NE)	43	8 (18.6)	35 (81.4)	NE (13.6, NE)	1.7885 (0.8301, 3.8534) 0.1377	0.1324	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9992
<65	289	72 (24.9)	217 (75.1)	NE (NE, NE)	126	30 (23.8)	96 (76.2)	NE (13.6, NE)	0.7675 (0.4976, 1.1838) 0.2314	0.2277	
>=65	82	20 (24.4)	62 (75.6)	NE (14.9, NE)	46	12 (26.1)	34 (73.9)	NE (6.9, NE)	0.7469 (0.3611, 1.5445) 0.4311	0.4326	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2032
<75	357	86 (24.1)	271 (75.9)	NE (NE, NE)	163	40 (24.5)	123 (75.5)	NE (13.6, NE)	0.7303 (0.4984, 1.0701) 0.1069	0.1047	
>=75	14	6 (42.9)	8 (57.1)	8.7 (3.0, NE)	9	2 (22.2)	7 (77.8)	NE (1.0, NE)	1.9222 (0.3865, 9.5603) 0.4246	0.4165	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.4225
White	175	37 (21.1)	138 (78.9)	NE (NE, NE)	85	15 (17.6)	70 (82.4)	NE (13.6, NE)	0.8543 (0.4635, 1.5744) 0.6136	0.6113	
Non-White	196	55 (28.1)	141 (71.9)	NE (NE, NE)	86	27 (31.4)	59 (68.6)	NE (6.9, NE)	0.6823 (0.4274, 1.0893) 0.1092	0.1071	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.5934
Asia	147	48 (32.7)	99 (67.3)	NE (14.9, NE)	63	21 (33.3)	42 (66.7)	NE (4.4, NE)	0.7049 (0.4181, 1.1884) 0.1894	0.1903	
North America	58	11 (19.0)	47 (81.0)	NE (NE, NE)	28	3 (10.7)	25 (89.3)	NE (NE, NE)	1.3604 (0.3751, 4.9339) 0.6397	0.6381	
Europe + Israel	166	33 (19.9)	133 (80.1)	NE (NE, NE)	81	18 (22.2)	63 (77.8)	NE (13.6, NE)	0.6668 (0.3715, 1.1968) 0.1744	0.1707	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.2936
0	199	50 (25.1)	149 (74.9)	NE (NE, NE)	95	19 (20.0)	76 (80.0)	NE (13.6, NE)	0.9303 (0.5440, 1.5909) 0.7918	0.7867	
1	172	42 (24.4)	130 (75.6)	NE (NE, NE)	77	23 (29.9)	54 (70.1)	NE (5.5, NE)	0.6302 (0.3757, 1.0571) 0.0802	0.0785	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.2901
0	60	16 (26.7)	44 (73.3)	NE (8.6, NE)	31	5 (16.1)	26 (83.9)	NE (NE, NE)	1.1447 (0.4110, 3.1880) 0.7959	0.7961	
1	107	32 (29.9)	75 (70.1)	NE (NE, NE)	48	13 (27.1)	35 (72.9)	NE (6.9, NE)	0.9375 (0.4908, 1.7908) 0.8449	0.8382	
2	114	25 (21.9)	89 (78.1)	NE (NE, NE)	50	11 (22.0)	39 (78.0)	NE (NE, NE)	0.7705 (0.3734, 1.5901) 0.4807	0.4731	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	19 (21.1)	71 (78.9)	NE (NE, NE)	43	13 (30.2)	30 (69.8)	NE (5.5, NE)	0.4562 (0.2188, 0.9511) 0.0363	0.0323	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.6311
PD	173	37 (21.4)	136 (78.6)	NE (NE, NE)	77	17 (22.1)	60 (77.9)	NE (NE, NE)	0.7530 (0.4209, 1.3474)	0.3341	
PR	48	10 (20.8)	38 (79.2)	NE (13.2, NE)	21	6 (28.6)	15 (71.4)	NE (3.4, NE)	0.3393 (0.1186, 1.0742)	0.0564	
SD	82	23 (28.0)	59 (72.0)	NE (NE, NE)	54	14 (25.9)	40 (74.1)	NE (NE, NE)	0.3569 (0.0668, 0.8962)	0.7619	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.5359
Yes	37	8 (21.6)	29 (78.4)	NE (13.2, NE)	13	4 (30.8)	9 (69.2)	NE (2.8, NE)	0.5212 (0.1530, 1.7755)	0.2802	
No	334	84 (25.1)	250 (74.9)	NE (NE, NE)	159	38 (23.9)	121 (76.1)	NE (13.6, NE)	0.2974 (0.5358, 1.1670)	0.2368	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.6090
Yes	24	6 (25.0)	18 (75.0)	NE (13.2, NE)	7	3 (42.9)	4 (57.1)	NE (1.4, NE)	0.6124 (0.1523, 2.4621) 0.4897	0.4675	
No	347	86 (24.8)	261 (75.2)	NE (NE, NE)	165	39 (23.6)	126 (76.4)	NE (13.6, NE)	0.7769 (0.5287, 1.1415) 0.1985	0.1982	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.6041
Normal Function	201	52 (25.9)	149 (74.1)	NE (NE, NE)	80	17 (21.3)	63 (78.8)	NE (NE, NE)	0.9639 (0.5529, 1.6803) 0.8968	0.8889	
Mild Impairment	123	30 (24.4)	93 (75.6)	NE (NE, NE)	65	14 (21.5)	51 (78.5)	NE (NE, NE)	0.7763 (0.4058, 1.4852) 0.4443	0.4468	
Moderate Impairment	41	10 (24.4)	31 (75.6)	NE (11.4, NE)	23	9 (39.1)	14 (60.9)	13.6 (3.3, NE)	0.5285 (0.2141, 1.3045) 0.1665	0.1597	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.4295
Normal Function	170	40 (23.5)	130 (76.5)	NE (NE, NE)	88	18 (20.5)	70 (79.5)	NE (13.6, NE)	0.8989 (0.5105, 1.5829) 0.7121	0.7082	
Mild Impairment	194	49 (25.3)	145 (74.7)	NE (NE, NE)	82	23 (28.0)	59 (72.0)	NE (6.9, NE)	0.6297 (0.3802, 1.0431) 0.0725	0.0707	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.7724
Yes	331	80 (24.2)	251 (75.8)	NE (NE, NE)	146	36 (24.7)	110 (75.3)	NE (13.6, NE)	0.7523 (0.5048, 1.1212) 0.1621	0.1607	
No	40	12 (30.0)	28 (70.0)	NE (7.9, NE)	26	6 (23.1)	20 (76.9)	NE (3.3, NE)	0.7895 (0.2813, 2.2155) 0.6535	0.6523	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.7163
Positive	329	80 (24.3)	249 (75.7)	NE (NE, NE)	152	37 (24.3)	115 (75.7)	NE (13.6, NE)	0.7502 (0.5051, 1.1143)	0.1536	
Negative	42	12 (28.6)	30 (71.4)	NE (8.7, NE)	20	5 (25.0)	15 (75.0)	NE (3.3, NE)	0.8202 (0.2757, 2.4402)	0.7251	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.8796
Positive	331	81 (24.5)	250 (75.5)	NE (NE, NE)	155	37 (23.9)	118 (76.1)	NE (13.6, NE)	0.7723 (0.5203, 1.1464)	0.1993	
Negative	40	11 (27.5)	29 (72.5)	NE (8.7, NE)	17	5 (29.4)	12 (70.6)	NE (2.2, NE)	0.6203 (0.2044, 1.8825)	0.3978	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.2073
HER2 IHC 1+	214	53 (24.8)	161 (75.2)	NE (NE, NE)	100	35 (35.0)	65 (65.0)	NE (NE, NE)	0.4859 (0.3153, 0.7487) 0.0011	0.0009	
HER2 IHC 2+/ISH Negative	157	28 (17.8)	129 (82.2)	24.8 (24.8, NE)	72	27 (37.5)	45 (62.5)	NE (3.5, NE)	0.3150 (0.1832, 0.5414) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.4543
1	220	48 (21.8)	172 (78.2)	NE (NE, NE)	94	31 (33.0)	63 (67.0)	NE (6.9, NE)	0.4533 (0.2870, 0.7160) 0.0007	0.0005	
>=2	150	33 (22.0)	117 (78.0)	24.8 (24.8, NE)	78	31 (39.7)	47 (60.3)	NE (2.4, NE)	0.3739 (0.2266, 0.6168) 0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.7798
Yes	233	40 (17.2)	193 (82.8)	NE (NE, NE)	112	35 (31.3)	77 (68.8)	NE (NE, NE)	0.4080 (0.2581, 0.6449) 0.0001	<0.0001	
No	98	35 (35.7)	63 (64.3)	24.8 (10.6, 24.8)	43	23 (53.5)	20 (46.5)	3.5 (0.5, NE)	0.4055 (0.2382, 0.6904) 0.0009	0.0007	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6467
<65	289	67 (23.2)	222 (76.8)	24.8 (24.8, NE)	126	45 (35.7)	81 (64.3)	NE (NE, NE)	0.4189 (0.2851, 0.6154) <0.0001	<0.0001	
>=65	82	14 (17.1)	68 (82.9)	NE (NE, NE)	46	17 (37.0)	29 (63.0)	NE (3.0, NE)	0.3539 (0.1733, 0.7227) 0.0043	0.0030	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8769
<75	357	79 (22.1)	278 (77.9)	24.8 (24.8, NE)	163	59 (36.2)	104 (63.8)	NE (6.9, NE)	0.4087 (0.2900, 0.5760) <0.0001	<0.0001	
>=75	14	2 (14.3)	12 (85.7)	NE (6.9, NE)	9	3 (33.3)	6 (66.7)	NE (0.2, NE)	0.3500 (0.0581, 2.1099) 0.2521	0.2311	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.7786
White	175	15 (8.6)	160 (91.4)	NE (NE, NE)	85	14 (16.5)	71 (83.5)	NE (NE, NE)	0.4059 (0.1942, 0.8485) 0.0165	0.0138	
Non-White	196	66 (33.7)	130 (66.3)	24.8 (11.8, NE)	86	48 (55.8)	38 (44.2)	1.0 (0.5, NE)	0.3447 (0.2361, 0.5033) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.0499
Asia	147	59 (40.1)	88 (59.9)	24.8 (9.7, NE)	63	45 (71.4)	18 (28.6)	0.5 (0.3, 0.5)	0.2554 (0.1714, 0.3805) <0.0001	<0.0001	
North America	58	10 (17.2)	48 (82.8)	NE (NE, NE)	28	12 (42.9)	16 (57.1)	NE (0.5, NE)	0.2396 (0.0998, 0.5752) 0.0014	0.0006	
Europe + Israel	166	12 (7.2)	154 (92.8)	NE (NE, NE)	81	5 (6.2)	76 (93.8)	NE (NE, NE)	0.9641 (0.3356, 2.7696) 0.9459	0.9453	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.0748
0	199	52 (26.1)	147 (73.9)	NE (NE, NE)	95	31 (32.6)	64 (67.4)	NE (NE, NE)	0.5311 (0.3388, 0.8324) 0.0058	0.0056	
1	172	29 (16.9)	143 (83.1)	24.8 (NE, NE)	77	31 (40.3)	46 (59.7)	6.9 (2.4, NE)	0.2967 (0.1767, 0.4982) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.7740
0	60	11 (18.3)	49 (81.7)	NE (NE, NE)	31	11 (35.5)	20 (64.5)	6.9 (2.4, NE)	0.3143 (0.1325, 0.7458)	0.0058	
1	107	26 (24.3)	81 (75.7)	NE (NE, NE)	48	17 (35.4)	31 (64.6)	NE (3.5, NE)	0.5289 (0.2865, 0.9763)	0.0388	
2	114	21 (18.4)	93 (81.6)	NE (NE, NE)	50	15 (30.0)	35 (70.0)	NE (NE, NE)	0.4260 (0.2166, 0.8379)	0.0121	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	23 (25.6)	67 (74.4)	24.8 (24.8, NE)	43	19 (44.2)	24 (55.8)	NE (0.5, NE)	0.3440 (0.1841, 0.6427) 0.0008	0.0006	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.4229
PD	173	33 (19.1)	140 (80.9)	NE (NE, NE)	77	24 (31.2)	53 (68.8)	NE (6.9, NE)	0.4386 (0.2577, 0.7464)	0.0019	
PR	48	11 (22.9)	37 (77.1)	24.8 (NE, NE)	21	10 (47.6)	11 (52.4)	NE (0.3, NE)	0.2214 (0.0889, 0.5514)	0.0005	
SD	82	20 (24.4)	62 (75.6)	NE (NE, NE)	54	22 (40.7)	32 (59.3)	NE (1.4, NE)	0.4704 (0.2561, 0.8641)	0.0137	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.8307
Yes	37	10 (27.0)	27 (73.0)	NE (NE, NE)	13	5 (38.5)	8 (61.5)	NE (0.3, NE)	0.4704 (0.1586, 1.3957)	0.1757	
No	334	71 (21.3)	263 (78.7)	24.8 (24.8, NE)	159	57 (35.8)	102 (64.2)	NE (6.9, NE)	0.3999 (0.2805, 0.5700)	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.1509
Yes	24	9 (37.5)	15 (62.5)	NE (4.2, NE)	7	2 (28.6)	5 (71.4)	NE (0.3, NE)	1.1276 (0.2421, 5.2510) 0.8784	0.8765	
No	347	72 (20.7)	275 (79.3)	24.8 (24.8, NE)	165	60 (36.4)	105 (63.6)	NE (6.9, NE)	0.3817 (0.2694, 0.5409) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.1044
Normal Function	201	48 (23.9)	153 (76.1)	NE (NE, NE)	80	27 (33.8)	53 (66.3)	NE (6.9, NE)	0.4478 (0.2765, 0.7252) 0.0011	0.0009	
Mild Impairment	123	28 (22.8)	95 (77.2)	24.8 (24.8, NE)	65	22 (33.8)	43 (66.2)	NE (NE, NE)	0.4748 (0.2690, 0.8378) 0.0102	0.0100	
Moderate Impairment	41	3 (7.3)	38 (92.7)	NE (NE, NE)	23	10 (43.5)	13 (56.5)	NE (0.9, NE)	0.1246 (0.0341, 0.4550) 0.0016	0.0002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.0597
Normal Function	170	36 (21.2)	134 (78.8)	NE (24.8, NE)	88	38 (43.2)	50 (56.8)	NE (2.4, NE)	0.3101 (0.1945, 0.4944) <0.0001	<0.0001	
Mild Impairment	194	43 (22.2)	151 (77.8)	NE (NE, NE)	82	22 (26.8)	60 (73.2)	NE (NE, NE)	0.5958 (0.3543, 1.0019) 0.0508	0.0538	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.2888
Yes	331	72 (21.8)	259 (78.2)	24.8 (NE, NE)	146	50 (34.2)	96 (65.8)	NE (NE, NE)	0.4398 (0.3051, 0.6340) <0.0001	<0.0001	
No	40	9 (22.5)	31 (77.5)	NE (NE, NE)	26	12 (46.2)	14 (53.8)	3.3 (0.5, NE)	0.2688 (0.1091, 0.6621) 0.0043	0.0024	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.8466
Positive	329	75 (22.8)	254 (77.2)	24.8 (24.8, NE)	152	57 (37.5)	95 (62.5)	NE (6.9, NE)	0.4048 (0.2854, 0.5742) <0.0001	<0.0001	
Negative	42	6 (14.3)	36 (85.7)	NE (NE, NE)	20	5 (25.0)	15 (75.0)	NE (2.4, NE)	0.3692 (0.1081, 1.2611) 0.1119	0.0991	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.5597
Positive	331	74 (22.4)	257 (77.6)	24.8 (24.8, NE)	155	58 (37.4)	97 (62.6)	NE (6.9, NE)	0.3996 (0.2819, 0.5664) <0.0001	<0.0001	
Negative	40	7 (17.5)	33 (82.5)	NE (NE, NE)	17	4 (23.5)	13 (76.5)	NE (2.4, NE)	0.4827 (0.1363, 1.7095) 0.2589	0.2494	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.3924
HER2 IHC 1+	214	51 (23.8)	163 (76.2)	NE (NE, NE)	100	29 (29.0)	71 (71.0)	NE (NE, NE)	0.5948 (0.3745, 0.9448) 0.0278	0.0284	
HER2 IHC 2+/ISH Negative	157	27 (17.2)	130 (82.8)	24.8 (24.8, NE)	72	20 (27.8)	52 (72.2)	NE (NE, NE)	0.4527 (0.2513, 0.8156) 0.0083	0.0072	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.4931
1	220	42 (19.1)	178 (80.9)	NE (NE, NE)	94	22 (23.4)	72 (76.6)	NE (NE, NE)	0.6115 (0.3631, 1.0298) 0.0644	0.0632	
>=2	150	36 (24.0)	114 (76.0)	24.8 (19.4, NE)	78	27 (34.6)	51 (65.4)	NE (NE, NE)	0.4814 (0.2889, 0.8021) 0.0050	0.0048	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											
Yes	233	34 (14.6)	199 (85.4)	NE (NE, NE)	112	25 (22.3)	87 (77.7)	NE (NE, NE)	0.5239 (0.3111, 0.8823) 0.0151	0.0140	0.4530
No	98	35 (35.7)	63 (64.3)	24.8 (9.2, 24.8)	43	17 (39.5)	26 (60.5)	NE (0.5, NE)	0.6416 (0.3578, 1.1507) 0.1365	0.1400	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8758
<65	289	63 (21.8)	226 (78.2)	24.8 (24.8, NE)	126	36 (28.6)	90 (71.4)	NE (NE, NE)	0.5329 (0.3512, 0.8086) 0.0031	0.0030	
>=65	82	15 (18.3)	67 (81.7)	NE (NE, NE)	46	13 (28.3)	33 (71.7)	NE (NE, NE)	0.5251 (0.2487, 1.1088) 0.0912	0.0858	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4832
<75	357	76 (21.3)	281 (78.7)	24.8 (24.8, NE)	163	48 (29.4)	115 (70.6)	NE (NE, NE)	0.5148 (0.3564, 0.7435) 0.0004	0.0004	
>=75	14	2 (14.3)	12 (85.7)	NE (4.2, NE)	9	1 (11.1)	8 (88.9)	NE (0.2, NE)	1.0628 (0.0954, 11.8437) 0.9605	0.9605	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.4607
White	175	14 (8.0)	161 (92.0)	NE (NE, NE)	85	13 (15.3)	72 (84.7)	NE (NE, NE)	0.4032 (0.1868, 0.8704) 0.0207	0.0173	
Non-White	196	64 (32.7)	132 (67.3)	24.8 (19.4, NE)	86	36 (41.9)	50 (58.1)	NE (1.2, NE)	0.5333 (0.3525, 0.8067) 0.0029	0.0027	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.7224
Asia	147	58 (39.5)	89 (60.5)	19.4 (8.3, NE)	63	33 (52.4)	30 (47.6)	3.2 (0.5, NE)	0.4524 (0.2929, 0.6990) 0.0004	0.0003	
North America	58	8 (13.8)	50 (86.2)	NE (NE, NE)	28	8 (28.6)	20 (71.4)	NE (NE, NE)	0.3628 (0.1342, 0.9809) 0.0457	0.0397	
Europe + Israel	166	12 (7.2)	154 (92.8)	NE (NE, NE)	81	8 (9.9)	73 (90.1)	NE (NE, NE)	0.6125 (0.2476, 1.5150) 0.2888	0.2837	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.2574
0	199	51 (25.6)	148 (74.4)	NE (NE, NE)	95	27 (28.4)	68 (71.6)	NE (NE, NE)	0.6159 (0.3842, 0.9873) 0.0441	0.0465	
1	172	27 (15.7)	145 (84.3)	24.8 (19.4, 24.8)	77	22 (28.6)	55 (71.4)	NE (NE, NE)	0.4424 (0.2494, 0.7850) 0.0053	0.0042	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.0540
0	60	13 (21.7)	47 (78.3)	NE (NE, NE)	31	11 (35.5)	20 (64.5)	NE (0.9, NE)	0.4244 (0.1878, 0.9591) 0.0394	0.0350	
1	107	24 (22.4)	83 (77.6)	NE (NE, NE)	48	13 (27.1)	35 (72.9)	NE (NE, NE)	0.6602 (0.3352, 1.3003) 0.2299	0.2265	
2	114	23 (20.2)	91 (79.8)	NE (19.4, NE)	50	7 (14.0)	43 (86.0)	NE (NE, NE)	1.1686 (0.4962, 2.7523) 0.7215	0.7206	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	18 (20.0)	72 (80.0)	NE (24.8, NE)	43	18 (41.9)	25 (58.1)	NE (0.5, NE)	0.2755 (0.1394, 0.5446) 0.0002	0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.7804
PD	173	37 (21.4)	136 (78.6)	NE (NE, NE)	77	22 (28.6)	55 (71.4)	NE (NE, NE)	0.5547 (0.3255, 0.9453)	0.0290	
PR	48	10 (20.8)	38 (79.2)	24.8 (19.4, 24.8)	21	7 (33.3)	14 (66.7)	NE (0.3, NE)	0.3448 (0.1236, 0.9618)	0.0357	
SD	82	18 (22.0)	64 (78.0)	NE (NE, NE)	54	16 (29.6)	38 (70.4)	NE (NE, NE)	0.5975 (0.3025, 1.1800)	0.1376	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.4618
Yes	37	12 (32.4)	25 (67.6)	NE (4.2, NE)	13	4 (30.8)	9 (69.2)	NE (0.4, NE)	0.8824 (0.2837, 2.7449)	0.8449	
No	334	66 (19.8)	268 (80.2)	24.8 (24.8, NE)	159	45 (28.3)	114 (71.7)	NE (NE, NE)	0.8290 (0.3372, 0.7297)	0.0003	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0619
Yes	24	9 (37.5)	15 (62.5)	NE (0.7, NE)	7	1 (14.3)	6 (85.7)	NE (0.4, NE)	2.7139 (0.3437, 21.4299) 0.3437	0.3280	
No	347	69 (19.9)	278 (80.1)	24.8 (24.8, NE)	165	48 (29.1)	117 (70.9)	NE (NE, NE)	0.4827 (0.3317, 0.7025) 0.0001	0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.2569
Normal Function	201	39 (19.4)	162 (80.6)	NE (NE, NE)	80	19 (23.8)	61 (76.3)	NE (NE, NE)	0.6095 (0.3497, 1.0625) 0.0808	0.0793	
Mild Impairment	123	31 (25.2)	92 (74.8)	24.8 (24.8, NE)	65	18 (27.7)	47 (72.3)	NE (NE, NE)	0.6839 (0.3793, 1.2331) 0.2065	0.2213	
Moderate Impairment	41	6 (14.6)	35 (85.4)	19.4 (19.4, NE)	23	9 (39.1)	14 (60.9)	NE (0.4, NE)	0.2362 (0.0788, 0.7075) 0.0099	0.0055	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.2314
Normal Function	170	40 (23.5)	130 (76.5)	24.8 (24.8, NE)	88	31 (35.2)	57 (64.8)	NE (NE, NE)	0.4629 (0.2866, 0.7478) 0.0016	0.0013	
Mild Impairment	194	36 (18.6)	158 (81.4)	NE (NE, NE)	82	16 (19.5)	66 (80.5)	NE (NE, NE)	0.7332 (0.4045, 1.3292) 0.3066	0.3160	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1112
Yes	331	68 (20.5)	263 (79.5)	24.8 (NE, NE)	146	37 (25.3)	109 (74.7)	NE (NE, NE)	0.6192 (0.4132, 0.9279) 0.0202	0.0206	
No	40	10 (25.0)	30 (75.0)	NE (19.4, NE)	26	12 (46.2)	14 (53.8)	NE (0.4, NE)	0.2716 (0.1096, 0.6734) 0.0049	0.0030	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.7942
Positive	329	68 (20.7)	261 (79.3)	24.8 (24.8, NE)	152	43 (28.3)	109 (71.7)	NE (NE, NE)	0.5332 (0.3621, 0.7850)	0.0013	
Negative	42	10 (23.8)	32 (76.2)	19.4 (8.5, NE)	20	6 (30.0)	14 (70.0)	NE (0.9, NE)	0.4982 (0.1705, 1.4555)	0.1952	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.4800
Positive	331	69 (20.8)	262 (79.2)	24.8 (24.8, NE)	155	42 (27.1)	113 (72.9)	NE (NE, NE)	0.5594 (0.3788, 0.8261)	0.0033	
Negative	40	9 (22.5)	31 (77.5)	NE (8.5, NE)	17	7 (41.2)	10 (58.8)	NE (0.5, NE)	0.3198 (0.1132, 0.9033)	0.0249	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0481
HER2 IHC 1+	214	42 (19.6)	172 (80.4)	NE (NE, NE)	100	31 (31.0)	69 (69.0)	NE (NE, NE)	0.4810 (0.2997, 0.7720) 0.0024	0.0020	
HER2 IHC 2+/ISH Negative	157	33 (21.0)	124 (79.0)	NE (NE, NE)	72	12 (16.7)	60 (83.3)	NE (13.6, NE)	1.0523 (0.5400, 2.0506) 0.8809	0.8872	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.9338
1	220	50 (22.7)	170 (77.3)	NE (NE, NE)	94	27 (28.7)	67 (71.3)	NE (NE, NE)	0.6355 (0.3952, 1.0218) 0.0614	0.0609	
>=2	150	25 (16.7)	125 (83.3)	NE (NE, NE)	78	16 (20.5)	62 (79.5)	NE (13.6, NE)	0.6237 (0.3298, 1.1797) 0.1466	0.1427	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.0678
Yes	233	39 (16.7)	194 (83.3)	NE (NE, NE)	112	29 (25.9)	83 (74.1)	NE (NE, NE)	0.5116 (0.3141, 0.8333) 0.0071	0.0062	
No	98	29 (29.6)	69 (70.4)	NE (NE, NE)	43	10 (23.3)	33 (76.7)	NE (13.6, NE)	1.0827 (0.5249, 2.2334) 0.8297	0.8319	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3179
<65	289	60 (20.8)	229 (79.2)	NE (NE, NE)	126	35 (27.8)	91 (72.2)	NE (13.6, NE)	0.5609 (0.3668, 0.8576) 0.0076	0.0068	
>=65	82	15 (18.3)	67 (81.7)	NE (NE, NE)	46	8 (17.4)	38 (82.6)	NE (NE, NE)	0.9727 (0.4103, 2.3060) 0.9499	0.9550	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6978
<75	357	72 (20.2)	285 (79.8)	NE (NE, NE)	163	41 (25.2)	122 (74.8)	NE (13.6, NE)	0.6295 (0.4263, 0.9297) 0.0200	0.0189	
>=75	14	3 (21.4)	11 (78.6)	NE (3.0, NE)	9	2 (22.2)	7 (77.8)	NE (0.5, NE)	0.9007 (0.1500, 5.4074) 0.9089	0.9089	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.7733
White	175	29 (16.6)	146 (83.4)	NE (NE, NE)	85	17 (20.0)	68 (80.0)	NE (13.6, NE)	0.6765 (0.3687, 1.2412) 0.2069	0.2057	
Non-White	196	46 (23.5)	150 (76.5)	NE (NE, NE)	86	26 (30.2)	60 (69.8)	NE (5.6, NE)	0.6016 (0.3692, 0.9803) 0.0414	0.0390	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.5709
Asia	147	39 (26.5)	108 (73.5)	NE (NE, NE)	63	23 (36.5)	40 (63.5)	NE (4.0, NE)	0.5203 (0.3076, 0.8801) 0.0148	0.0131	
North America	58	6 (10.3)	52 (89.7)	NE (NE, NE)	28	2 (7.1)	26 (92.9)	NE (NE, NE)	1.0406 (0.2042, 5.3018) 0.9618	0.9582	
Europe + Israel	166	30 (18.1)	136 (81.9)	NE (NE, NE)	81	18 (22.2)	63 (77.8)	NE (13.6, NE)	0.7071 (0.3919, 1.2759) 0.2497	0.2461	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.5984
0	199	42 (21.1)	157 (78.9)	NE (NE, NE)	95	22 (23.2)	73 (76.8)	NE (13.6, NE)	0.7036 (0.4171, 1.1869) 0.1876	0.1886	
1	172	33 (19.2)	139 (80.8)	NE (NE, NE)	77	21 (27.3)	56 (72.7)	NE (5.5, NE)	0.5851 (0.3359, 1.0192) 0.0584	0.0546	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.9258
0	60	11 (18.3)	49 (81.7)	NE (NE, NE)	31	7 (22.6)	24 (77.4)	NE (4.0, NE)	0.6383 (0.2427, 1.6788)	0.3609	
1	107	27 (25.2)	80 (74.8)	NE (NE, NE)	48	15 (31.3)	33 (68.8)	NE (13.6, NE)	0.6843 (0.3633, 1.2889)	0.2352	
2	114	22 (19.3)	92 (80.7)	NE (NE, NE)	50	11 (22.0)	39 (78.0)	NE (5.6, NE)	0.7381 (0.3540, 1.5388)	0.4139	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	15 (16.7)	75 (83.3)	NE (NE, NE)	43	10 (23.3)	33 (76.7)	NE (5.5, NE)	0.4910 (0.2146, 1.1237) 0.0922	0.0869	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.6316
PD	173	34 (19.7)	139 (80.3)	NE (NE, NE)	77	18 (23.4)	59 (76.6)	NE (NE, NE)	0.6574 (0.3682, 1.1737)	0.1534	
PR	48	9 (18.8)	39 (81.3)	NE (NE, NE)	21	7 (33.3)	14 (66.7)	NE (3.4, NE)	0.3753 (0.1327, 1.0614)	0.0546	
SD	82	16 (19.5)	66 (80.5)	NE (NE, NE)	54	12 (22.2)	42 (77.8)	NE (NE, NE)	0.7751 (0.3647, 1.6474)	0.5028	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.6286
Yes	37	6 (16.2)	31 (83.8)	NE (NE, NE)	13	2 (15.4)	11 (84.6)	NE (2.8, NE)	0.9563 (0.1914, 4.7777)	0.9325	
No	334	69 (20.7)	265 (79.3)	NE (NE, NE)	159	41 (25.8)	118 (74.2)	NE (13.6, NE)	0.9566 (0.4235, 0.9282)	0.0191	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.6411
Yes	24	6 (25.0)	18 (75.0)	NE (NE, NE)	7	2 (28.6)	5 (71.4)	NE (2.8, NE)	0.9634 (0.1943, 4.7767) 0.9636	0.9282	
No	347	69 (19.9)	278 (80.1)	NE (NE, NE)	165	41 (24.8)	124 (75.2)	NE (13.6, NE)	0.6223 (0.4203, 0.9216) 0.0179	0.0173	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.8540
Normal Function	201	48 (23.9)	153 (76.1)	NE (NE, NE)	80	23 (28.8)	57 (71.3)	NE (5.6, NE)	0.6643 (0.4010, 1.1005) 0.1123	0.1081	
Mild Impairment	123	21 (17.1)	102 (82.9)	NE (NE, NE)	65	12 (18.5)	53 (81.5)	NE (NE, NE)	0.7333 (0.3573, 1.5049) 0.3977	0.3982	
Moderate Impairment	41	6 (14.6)	35 (85.4)	NE (NE, NE)	23	6 (26.1)	17 (73.9)	NE (13.6, NE)	0.4721 (0.1511, 1.4747) 0.1965	0.1843	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.9503
Normal Function	170	28 (16.5)	142 (83.5)	NE (NE, NE)	88	18 (20.5)	70 (79.5)	NE (13.6, NE)	0.6359 (0.3478, 1.1626) 0.1414	0.1372	
Mild Impairment	194	46 (23.7)	148 (76.3)	NE (NE, NE)	82	24 (29.3)	58 (70.7)	NE (5.6, NE)	0.6322 (0.3834, 1.0425) 0.0723	0.0706	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.6763
Yes	331	65 (19.6)	266 (80.4)	NE (NE, NE)	146	37 (25.3)	109 (74.7)	NE (13.6, NE)	0.6283 (0.4176, 0.9452) 0.0257	0.0247	
No	40	10 (25.0)	30 (75.0)	NE (10.4, NE)	26	6 (23.1)	20 (76.9)	NE (4.0, NE)	0.7640 (0.2685, 2.1734) 0.6138	0.6098	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.8554
Positive	329	68 (20.7)	261 (79.3)	NE (NE, NE)	152	39 (25.7)	113 (74.3)	NE (13.6, NE)	0.6360 (0.4267, 0.9479)	0.0254	
Negative	42	7 (16.7)	35 (83.3)	NE (NE, NE)	20	4 (20.0)	16 (80.0)	NE (4.0, NE)	0.7215 (0.2069, 2.5158)	0.6103	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.9384
Positive	331	68 (20.5)	263 (79.5)	NE (NE, NE)	155	39 (25.2)	116 (74.8)	NE (13.6, NE)	0.6474 (0.4343, 0.9650)	0.0318	
Negative	40	7 (17.5)	33 (82.5)	NE (NE, NE)	17	4 (23.5)	13 (76.5)	NE (4.0, NE)	0.6219 (0.1777, 2.1768)	0.4569	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.1996
HER2 IHC 1+	214	44 (20.6)	170 (79.4)	NE (NE, NE)	100	5 (5.0)	95 (95.0)	NE (NE, NE)	3.4592 (1.3648, 8.7678) 0.0089	0.0056	
HER2 IHC 2+/ISH Negative	157	29 (18.5)	128 (81.5)	NE (NE, NE)	72	7 (9.7)	65 (90.3)	NE (NE, NE)	1.5055 (0.6531, 3.4707) 0.3370	0.3340	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting									0.4946
1	220	35 (15.9)	185 (84.1) NE (NE, NE)	94	4 (4.3)	90 (95.7) NE (NE, NE)	2.9940 (1.0579, 8.4730) 0.0388	0.0308	
>=2	150	38 (25.3)	112 (74.7) NE (NE, NE)	78	8 (10.3)	70 (89.7) NE (NE, NE)	2.0828 (0.9636, 4.5020) 0.0621	0.0577	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											
Yes	233	39 (16.7)	194 (83.3)	NE (NE, NE)	112	5 (4.5)	107 (95.5)	NE (NE, NE)	2.9864 (1.1679, 7.6364) 0.0224	0.0168	0.8594
No	98	28 (28.6)	70 (71.4)	NE (NE, NE)	43	4 (9.3)	39 (90.7)	NE (NE, NE)	2.7272 (0.9522, 7.8105) 0.0617	0.0527	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0564
<65	289	60 (20.8)	229 (79.2)	NE (NE, NE)	126	6 (4.8)	120 (95.2)	NE (NE, NE)	3.4583 (1.4861, 8.0477) 0.0040	0.0022	
>=65	82	13 (15.9)	69 (84.1)	NE (NE, NE)	46	6 (13.0)	40 (87.0)	NE (NE, NE)	1.0966 (0.4126, 2.9149) 0.8533	0.8565	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0038
<75	357	71 (19.9)	286 (80.1)	NE (NE, NE)	163	8 (4.9)	155 (95.1)	NE (NE, NE)	3.3409 (1.6015, 6.9695) 0.0013	0.0006	
>=75	14	2 (14.3)	12 (85.7)	NE (4.0, NE)	9	4 (44.4)	5 (55.6)	NE (0.5, NE)	0.2168 (0.0384, 1.2246) 0.0835	0.0593	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.0780
White	175	18 (10.3)	157 (89.7)	NE (NE, NE)	85	6 (7.1)	79 (92.9)	NE (NE, NE)	1.0917 (0.4266, 2.7938) 0.8548	0.8558	
Non-White	196	55 (28.1)	141 (71.9)	NE (NE, NE)	86	6 (7.0)	80 (93.0)	NE (NE, NE)	3.4549 (1.4816, 8.0560) 0.0041	0.0023	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.3024
Asia	147	51 (34.7)	96 (65.3)	NE (12.8, NE)	63	6 (9.5)	57 (90.5)	NE (NE, NE)	3.2337 (1.3820, 7.5666) 0.0068	0.0044	
North America	58	7 (12.1)	51 (87.9)	NE (NE, NE)	28	3 (10.7)	25 (89.3)	NE (NE, NE)	0.9457 (0.2433, 3.6756) 0.9358	0.9354	
Europe + Israel	166	15 (9.0)	151 (91.0)	NE (NE, NE)	81	3 (3.7)	78 (96.3)	NE (NE, NE)	1.6409 (0.4644, 5.7972) 0.4419	0.4369	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.6915
0	199	46 (23.1)	153 (76.9)	NE (NE, NE)	95	7 (7.4)	88 (92.6)	NE (NE, NE)	2.6572 (1.1929, 5.9186) 0.0168	0.0134	
1	172	27 (15.7)	145 (84.3)	NE (NE, NE)	77	5 (6.5)	72 (93.5)	NE (NE, NE)	1.8742 (0.7133, 4.9243) 0.2025	0.1972	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.4490
0	60	7 (11.7)	53 (88.3)	NE (NE, NE)	31	3 (9.7)	28 (90.3)	NE (NE, NE)	1.1499 (0.2966, 4.4576) 0.8399	0.8528	
1	107	25 (23.4)	82 (76.6)	NE (NE, NE)	48	3 (6.3)	45 (93.8)	NE (NE, NE)	3.3244 (1.0021, 11.0280) 0.0496	0.0375	
2	114	22 (19.3)	92 (80.7)	NE (NE, NE)	50	2 (4.0)	48 (96.0)	NE (NE, NE)	3.5989 (0.8323, 15.5613) 0.0865	0.0684	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2)									
>=3	90	19 (21.1)	71 (78.9)	43	4 (9.3)	39 (90.7)	1.9330 (0.6491, 5.7564) 0.2365	0.2311	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.6353
PD	173	29 (16.8)	144 (83.2)	NE (NE, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	3.5413 (1.0728, 11.6901)	0.0269	
PR	48	9 (18.8)	39 (81.3)	NE (NE, NE)	21	1 (4.8)	20 (95.2)	NE (NE, NE)	0.0380 (0.4826, 30.2103)	0.1725	
SD	82	16 (19.5)	66 (80.5)	NE (NE, NE)	54	5 (9.3)	49 (90.7)	NE (NE, NE)	0.2043 (0.6661, 5.0860)	0.2369	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.4671
Yes	37	9 (24.3)	28 (75.7)	NE (NE, NE)	13	2 (15.4)	11 (84.6)	NE (NE, NE)	1.4904 (0.3206, 6.9289)	0.6107	0.6084
No	334	64 (19.2)	270 (80.8)	NE (NE, NE)	159	10 (6.3)	149 (93.7)	NE (NE, NE)	2.4324 (1.2414, 4.7659)	0.0096	0.0078

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.2844
Yes	24	5 (20.8)	19 (79.2)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9956	0.2096	
No	347	68 (19.6)	279 (80.4)	NE (NE, NE)	165	12 (7.3)	153 (92.7)	NE (NE, NE)	2.1685 (1.1668, 4.0301) 0.0144	0.0127	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0012
Normal Function	201	39 (19.4)	162 (80.6)	NE (NE, NE)	80	2 (2.5)	78 (97.5)	NE (NE, NE)	5.7264 (1.3732, 23.8804) 0.0166	0.0067	
Mild Impairment	123	27 (22.0)	96 (78.0)	NE (NE, NE)	65	3 (4.6)	62 (95.4)	NE (NE, NE)	4.4651 (1.3489, 14.7801) 0.0143	0.0071	
Moderate Impairment	41	6 (14.6)	35 (85.4)	NE (NE, NE)	23	7 (30.4)	16 (69.6)	NE (3.7, NE)	0.3848 (0.1289, 1.1488) 0.0870	0.0765	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.9519
Normal Function	170	28 (16.5)	142 (83.5)	NE (NE, NE)	88	5 (5.7)	83 (94.3)	NE (NE, NE)	2.2869 (0.8743, 5.9823) 0.0918	0.0842	
Mild Impairment	194	44 (22.7)	150 (77.3)	NE (NE, NE)	82	7 (8.5)	75 (91.5)	NE (NE, NE)	2.1864 (0.9781, 4.8874) 0.0566	0.0529	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.9475
Yes	331	63 (19.0)	268 (81.0)	NE (NE, NE)	146	10 (6.8)	136 (93.2)	NE (NE, NE)	2.2346 (1.1403, 4.3790) 0.0192	0.0168	
No	40	10 (25.0)	30 (75.0)	NE (NE, NE)	26	2 (7.7)	24 (92.3)	NE (NE, NE)	3.1199 (0.6817, 14.2792) 0.1426	0.1227	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.0976
Positive	329	67 (20.4)	262 (79.6)	NE (NE, NE)	152	9 (5.9)	143 (94.1)	NE (NE, NE)	2.8312 (1.4052, 5.7045) 0.0036	0.0024	
Negative	42	6 (14.3)	36 (85.7)	NE (NE, NE)	20	3 (15.0)	17 (85.0)	NE (NE, NE)	0.7598 (0.1813, 3.1838) 0.7071	0.6985	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Run date: 13SEP2022 – 17:37; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_AESOCPT10PAT\_2\_SAS.rtf

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.0952
Positive	331	66 (19.9)	265 (80.1)	NE (NE, NE)	155	9 (5.8)	146 (94.2)	NE (NE, NE)	2.8325 (1.4047, 5.7116)	0.0025	
Negative	40	7 (17.5)	33 (82.5)	NE (NE, NE)	17	3 (17.6)	14 (82.4)	NE (NE, NE)	0.7344 (0.1819, 2.9646)	0.6565	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Weight decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.5460
HER2 IHC 1+	214	35 (16.4)	179 (83.6)	NE (NE, NE)	100	7 (7.0)	93 (93.0)	NE (NE, NE)	1.6029 (0.7063, 3.6377) 0.2592	0.2553	
HER2 IHC 2+/ISH Negative	157	25 (15.9)	132 (84.1)	NE (NE, NE)	72	7 (9.7)	65 (90.3)	NE (7.9, NE)	0.9838 (0.4186, 2.3122) 0.9701	0.9685	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Weight decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.5447
1	220	33 (15.0)	187 (85.0)	NE (NE, NE)	94	6 (6.4)	88 (93.6)	NE (NE, NE)	1.5203 (0.6300, 3.6686) 0.3513	0.3480	
>=2	150	27 (18.0)	123 (82.0)	NE (NE, NE)	78	8 (10.3)	70 (89.7)	NE (NE, NE)	1.1345 (0.5088, 2.5297) 0.7578	0.7588	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Weight decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.9466
Yes	233	33 (14.2)	200 (85.8)	NE (NE, NE)	112	7 (6.3)	105 (93.8)	NE (NE, NE)	1.4532 (0.6361, 3.3200) 0.3752	0.3734	
No	98	22 (22.4)	76 (77.6)	NE (NE, NE)	43	5 (11.6)	38 (88.4)	NE (NE, NE)	1.2729 (0.4780, 3.3897) 0.6292	0.6283	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Investigations; PT: Weight decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0431
<65	289	42 (14.5)	247 (85.5)	NE (NE, NE)	126	12 (9.5)	114 (90.5)	NE (NE, NE)	0.9565 (0.4977, 1.8383) 0.8939	0.8940	
>=65	82	18 (22.0)	64 (78.0)	NE (15.5, NE)	46	2 (4.3)	44 (95.7)	NE (NE, NE)	3.7198 (0.8572, 16.1420) 0.0794	0.0601	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Investigations; PT: Weight decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9533
<75	357	58 (16.2)	299 (83.8)	NE (NE, NE)	163	13 (8.0)	150 (92.0)	NE (NE, NE)	1.2836 (0.6972, 2.3632) 0.4226	0.4222	
>=75	14	2 (14.3)	12 (85.7)	NE (2.8, NE)	9	1 (11.1)	8 (88.9)	NE (4.6, NE)	1.3612 (0.1233, 15.0278) 0.8013	0.8005	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.0584
White	175	28 (16.0)	147 (84.0)	NE (NE, NE)	85	3 (3.5)	82 (96.5)	NE (NE, NE)	2.9564 (0.8923, 9.7951) 0.0761	0.0630	
Non-White	196	32 (16.3)	164 (83.7)	NE (NE, NE)	86	11 (12.8)	75 (87.2)	NE (NE, NE)	0.8209 (0.4077, 1.6532) 0.5806	0.5797	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.2344
Asia	147	27 (18.4)	120 (81.6)	NE (NE, NE)	63	9 (14.3)	54 (85.7)	NE (NE, NE)	0.7309 (0.3368, 1.5862) 0.4278	0.4255	
North America	58	10 (17.2)	48 (82.8)	NE (NE, NE)	28	2 (7.1)	26 (92.9)	NE (7.9, NE)	1.4249 (0.3051, 6.6547) 0.6525	0.6506	
Europe + Israel	166	23 (13.9)	143 (86.1)	NE (NE, NE)	81	3 (3.7)	78 (96.3)	NE (NE, NE)	2.7890 (0.8315, 9.3549) 0.0967	0.0829	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Investigations; PT: Weight decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.5247
0	199	26 (13.1)	173 (86.9)	NE (NE, NE)	95	7 (7.4)	88 (92.6)	NE (NE, NE)	1.0039 (0.4283, 2.3535) 0.9928	0.9947	
1	172	34 (19.8)	138 (80.2)	NE (NE, NE)	77	7 (9.1)	70 (90.9)	NE (7.9, NE)	1.6408 (0.7225, 3.7263) 0.2367	0.2327	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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SOC: Investigations; PT: Weight decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.8493
0	60	8 (13.3)	52 (86.7)	NE (NE, NE)	31	3 (9.7)	28 (90.3)	NE (5.2, NE)	0.9899 (0.2540, 3.8585) 0.9884	0.9910	
1	107	18 (16.8)	89 (83.2)	NE (NE, NE)	48	5 (10.4)	43 (89.6)	NE (NE, NE)	1.1986 (0.4425, 3.2464) 0.7217	0.7216	
2	114	20 (17.5)	94 (82.5)	NE (NE, NE)	50	3 (6.0)	47 (94.0)	NE (NE, NE)	2.1558 (0.6363, 7.3045) 0.2173	0.2066	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.8.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Investigations; PT: Weight decreased

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 (15.6)	76 (84.4)	NE (NE, NE)	43 (7.0)	40 (93.0)	NE (7.2, NE)	1.0618 (0.2952, 3.8189) 0.9269	0.9279	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Weight decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.9788
PD	173	26 (15.0)	147 (85.0)	NE (NE, NE)	77	6 (7.8)	71 (92.2)	NE (NE, NE)	1.2279 (0.4986, 3.0239) 0.6553	0.6551	
PR	48	5 (10.4)	43 (89.6)	NE (NE, NE)	21	1 (4.8)	20 (95.2)	NE (NE, NE)	1.5981 (0.1846, 13.8347) 0.6703	0.6675	
SD	82	12 (14.6)	70 (85.4)	NE (NE, NE)	54	5 (9.3)	49 (90.7)	NE (7.2, NE)	1.1142 (0.3873, 3.2055) 0.8410	0.8410	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Weight decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.1158
Yes	37	7 (18.9)	30 (81.1)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9946	0.1209	
No	334	53 (15.9)	281 (84.1)	NE (NE, NE)	159	14 (8.8)	145 (91.2)	NE (NE, NE)	1.1112 (0.6109, 2.0210) 0.7298	0.7313	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Weight decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.1493
Yes	24	5 (20.8)	19 (79.2)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9955	0.1906	
No	347	55 (15.9)	292 (84.1)	NE (NE, NE)	165	14 (8.5)	151 (91.5)	NE (NE, NE)	1.1460 (0.6315, 2.0797) 0.6540	0.6550	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Weight decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.2458
Normal Function	201	31 (15.4)	170 (84.6)	NE (NE, NE)	80	9 (11.3)	71 (88.8)	NE (7.9, NE)	0.8753 (0.4095, 1.8706) 0.7310	0.7297	
Mild Impairment	123	18 (14.6)	105 (85.4)	NE (NE, NE)	65	3 (4.6)	62 (95.4)	NE (NE, NE)	1.9828 (0.5755, 6.8311) 0.2781	0.2693	
Moderate Impairment	41	11 (26.8)	30 (73.2)	NE (10.3, NE)	23	2 (8.7)	21 (91.3)	NE (NE, NE)	2.5684 (0.5675, 11.6243) 0.2208	0.2041	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Weight decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.2670
Normal Function	170	30 (17.6)	140 (82.4)	NE (NE, NE)	88	10 (11.4)	78 (88.6)	NE (NE, NE)	0.9945 (0.4796, 2.0624) 0.9882	0.9877	
Mild Impairment	194	30 (15.5)	164 (84.5)	NE (NE, NE)	82	4 (4.9)	78 (95.1)	NE (7.9, NE)	2.0743 (0.7242, 5.9415) 0.1742	0.1653	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Weight decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1187
Yes	331	56 (16.9)	275 (83.1)	NE (NE, NE)	146	11 (7.5)	135 (92.5)	NE (NE, NE)	1.5736 (0.8198, 3.0203) 0.1730	0.1697	
No	40	4 (10.0)	36 (90.0)	NE (NE, NE)	26	3 (11.5)	23 (88.5)	NE (5.2, NE)	0.2264 (0.0421, 1.2169) 0.0834	0.0659	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Weight decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.5317
Positive	329	55 (16.7)	274 (83.3)	NE (NE, NE)	152	12 (7.9)	140 (92.1)	NE (NE, NE)	1.3430 (0.7138, 2.5267) 0.3605	0.3593	
Negative	42	5 (11.9)	37 (88.1)	NE (NE, NE)	20	2 (10.0)	18 (90.0)	NE (NE, NE)	1.1019 (0.2127, 5.7074) 0.9079	0.9059	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Weight decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.3966
Positive	331	55 (16.6)	276 (83.4)	NE (NE, NE)	155	12 (7.7)	143 (92.3)	NE (NE, NE)	1.3673 (0.7266, 2.5731) 0.3321	0.3305	
Negative	40	5 (12.5)	35 (87.5)	NE (NE, NE)	17	2 (11.8)	15 (88.2)	NE (3.0, NE)	0.9284 (0.1786, 4.8251) 0.9296	0.9318	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood alkaline phosphatase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0123
HER2 IHC 1+	214	18 (8.4)	196 (91.6)	NE (NE, NE)	100	5 (5.0)	95 (95.0)	NE (NE, NE)	1.3601 (0.5028, 3.6791) 0.5447	0.5427	
HER2 IHC 2+/ISH Negative	157	18 (11.5)	139 (88.5)	NE (NE, NE)	72	0	72 (100)	NE (NE, NE)	NE (NE, NE) 0.9920	0.0232	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood alkaline phosphatase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.5342
1	220	17 (7.7)	203 (92.3)	NE (NE, NE)	94	3 (3.2)	91 (96.8)	NE (NE, NE)	1.8982 (0.5531, 6.5146) 0.3084	0.3000	
>=2	150	19 (12.7)	131 (87.3)	NE (NE, NE)	78	2 (2.6)	76 (97.4)	NE (NE, NE)	3.2539 (0.7515, 14.0895) 0.1146	0.0948	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood alkaline phosphatase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.9405
Yes	233	18 (7.7)	215 (92.3)	NE (NE, NE)	112	2 (1.8)	110 (98.2)	NE (NE, NE)	3.0779 (0.7084, 13.3742) 0.1336	0.1143	
No	98	16 (16.3)	82 (83.7)	NE (NE, NE)	43	2 (4.7)	41 (95.3)	NE (NE, NE)	2.8344 (0.6502, 12.3550) 0.1655	0.1468	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Blood alkaline phosphatase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5902
<65	289	28 (9.7)	261 (90.3)	NE (NE, NE)	126	4 (3.2)	122 (96.8)	NE (NE, NE)	2.0967 (0.7303, 6.0196) 0.1689	0.1591	
>=65	82	8 (9.8)	74 (90.2)	NE (NE, NE)	46	1 (2.2)	45 (97.8)	NE (NE, NE)	3.7549 (0.4668, 30.2057) 0.2136	0.1819	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Blood alkaline phosphatase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3292
<75	357	34 (9.5)	323 (90.5)	NE (NE, NE)	163	5 (3.1)	158 (96.9)	NE (NE, NE)	2.2604 (0.8791, 5.8124) 0.0905	0.0819	
>=75	14	2 (14.3)	12 (85.7)	NE (6.2, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9978	0.2614	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood alkaline phosphatase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.8286
White	175	16 (9.1)	159 (90.9)	NE (NE, NE)	85	2 (2.4)	83 (97.6)	NE (NE, NE)	2.4851 (0.5638, 10.9543) 0.2291	0.2132	
Non-White	196	20 (10.2)	176 (89.8)	NE (NE, NE)	86	3 (3.5)	83 (96.5)	NE (NE, NE)	2.3349 (0.6912, 7.8870) 0.1721	0.1598	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Blood alkaline phosphatase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.4056
Asia	147	18 (12.2)	129 (87.8)	NE (NE, NE)	63	3 (4.8)	60 (95.2)	NE (NE, NE)	1.9072 (0.5591, 6.5058) 0.3024	0.2944	
North America	58	6 (10.3)	52 (89.7)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9948	0.1202	
Europe + Israel	166	12 (7.2)	154 (92.8)	NE (NE, NE)	81	2 (2.5)	79 (97.5)	NE (NE, NE)	1.8595 (0.4083, 8.4673) 0.4226	0.4155	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood alkaline phosphatase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.7924
0	199	17 (8.5)	182 (91.5)	NE (NE, NE)	95	2 (2.1)	93 (97.9)	NE (NE, NE)	2.4947 (0.5733, 10.8554) 0.2230	0.2072	
1	172	19 (11.0)	153 (89.0)	NE (NE, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	2.3836 (0.7006, 8.1098) 0.1644	0.1516	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood alkaline phosphatase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.2665
0	60	4 (6.7)	56 (93.3)	NE (NE, NE)	31	2 (6.5)	29 (93.5)	NE (NE, NE)	0.6398 (0.1132, 3.6151) 0.6132	0.6108	
1	107	18 (16.8)	89 (83.2)	NE (NE, NE)	48	2 (4.2)	46 (95.8)	NE (NE, NE)	3.6731 (0.8513, 15.8487) 0.0811	0.0615	
2	114	6 (5.3)	108 (94.7)	NE (NE, NE)	50	1 (2.0)	49 (98.0)	NE (NE, NE)	1.9662 (0.2337, 16.5423) 0.5338	0.5262	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood alkaline phosphatase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	8 (8.9)	82 (91.1)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9951	0.1799	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood alkaline phosphatase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.7253
PD	173	15 (8.7)	158 (91.3)	NE (NE, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	1.7342 (0.4991, 6.0253)	0.3795	
PR	48	2 (4.2)	46 (95.8)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	NE (NE, NE)	0.5145	
SD	82	8 (9.8)	74 (90.2)	NE (NE, NE)	54	2 (3.7)	52 (96.3)	NE (NE, NE)	2.0349 (0.4284, 9.6651)	0.3618	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood alkaline phosphatase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.2879
Yes	37	3 (8.1)	34 (91.9)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	0.7614 (0.0776, 7.4691)	0.8145	
No	334	33 (9.9)	301 (90.1)	NE (NE, NE)	159	4 (2.5)	155 (97.5)	NE (NE, NE)	2.8659 (1.0102, 8.1306)	0.0385	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood alkaline phosphatase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.1107
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	1 (14.3)	6 (85.7)	NE (0.3, NE)	0.2546 (0.0158, 4.0964) 0.3345	0.2977	
No	347	35 (10.1)	312 (89.9)	NE (NE, NE)	165	4 (2.4)	161 (97.6)	NE (NE, NE)	3.0174 (1.0672, 8.5320) 0.0373	0.0286	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Blood alkaline phosphatase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.6398
Normal Function	201	20 (10.0)	181 (90.0)	NE (NE, NE)	80	3 (3.8)	77 (96.3)	NE (NE, NE)	1.9672 (0.5805, 6.6657) 0.2772	0.2677	
Mild Impairment	123	13 (10.6)	110 (89.4)	NE (NE, NE)	65	1 (1.5)	64 (98.5)	NE (NE, NE)	4.4471 (0.5760, 34.3339) 0.1524	0.1175	
Moderate Impairment	41	3 (7.3)	38 (92.7)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	1.5282 (0.1585, 14.7298) 0.7137	0.7115	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood alkaline phosphatase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.6000
Normal Function	170	15 (8.8)	155 (91.2)	NE (NE, NE)	88	3 (3.4)	85 (96.6)	NE (NE, NE)	1.9341 (0.5548, 6.7423) 0.3005	0.2919	
Mild Impairment	194	21 (10.8)	173 (89.2)	NE (NE, NE)	82	2 (2.4)	80 (97.6)	NE (NE, NE)	3.0854 (0.7193, 13.2355) 0.1294	0.1099	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Blood alkaline phosphatase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.9753
Yes	331	30 (9.1)	301 (90.9)	NE (NE, NE)	146	4 (2.7)	142 (97.3)	NE (NE, NE)	2.5318 (0.8883, 7.2158) 0.0821	0.0716	
No	40	6 (15.0)	34 (85.0)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	2.0321 (0.2344, 17.6213) 0.5200	0.5118	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Investigations; PT: Blood alkaline phosphatase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.4399
Positive	329	33 (10.0)	296 (90.0)	NE (NE, NE)	152	4 (2.6)	148 (97.4)	NE (NE, NE)	2.8341 (0.9997, 8.0342)	0.0405	
Negative	42	3 (7.1)	39 (92.9)	NE (NE, NE)	20	1 (5.0)	19 (95.0)	NE (4.0, NE)	0.8582 (0.0841, 8.7565)	0.8973	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Blood alkaline phosphatase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.2471
Positive	331	34 (10.3)	297 (89.7)	NE (NE, NE)	155	4 (2.6)	151 (97.4)	NE (NE, NE)	2.9362 (1.0373, 8.3108)	0.0333	
Negative	40	2 (5.0)	38 (95.0)	NE (NE, NE)	17	1 (5.9)	16 (94.1)	NE (4.0, NE)	0.5822 (0.0507, 6.6805)	0.6603	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0408
HER2 IHC 1+	214	19 (8.9)	195 (91.1)	NE (NE, NE)	100	4 (4.0)	96 (96.0)	NE (NE, NE)	1.8657 (0.6302, 5.5234) 0.2601	0.2539	
HER2 IHC 2+/ISH Negative	157	10 (6.4)	147 (93.6)	NE (24.8, NE)	72	8 (11.1)	64 (88.9)	NE (NE, NE)	0.4274 (0.1638, 1.1151) 0.0823	0.0740	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.5314
1	220	16 (7.3)	204 (92.7)	NE (NE, NE)	94	5 (5.3)	89 (94.7)	NE (NE, NE)	1.2460 (0.4555, 3.4080) 0.6684	0.6682	
>=2	150	13 (8.7)	137 (91.3)	NE (24.8, NE)	78	7 (9.0)	71 (91.0)	NE (NE, NE)	0.6390 (0.2456, 1.6624) 0.3585	0.3536	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.0357
Yes	233	12 (5.2)	221 (94.8)	NE (NE, NE)	112	8 (7.1)	104 (92.9)	NE (NE, NE)	0.5862 (0.2371, 1.4490) 0.2474	0.2429	
No	98	12 (12.2)	86 (87.8)	NE (24.8, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	4.5315 (0.5841, 35.1571) 0.1483	0.1130	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8239
<65	289	20 (6.9)	269 (93.1)	NE (24.8, NE)	126	7 (5.6)	119 (94.4)	NE (NE, NE)	0.9893 (0.4125, 2.3730) 0.9808	0.9785	
>=65	82	9 (11.0)	73 (89.0)	NE (NE, NE)	46	5 (10.9)	41 (89.1)	NE (NE, NE)	0.8864 (0.2959, 2.6549) 0.8294	0.8307	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0603
<75	357	26 (7.3)	331 (92.7)	NE (24.8, NE)	163	12 (7.4)	151 (92.6)	NE (NE, NE)	0.7794 (0.3887, 1.5627) 0.4826	0.4796	
>=75	14	3 (21.4)	11 (78.6)	NE (3.5, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9973	0.1455	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.6159
White	175	9 (5.1)	166 (94.9)	NE (NE, NE)	85	5 (5.9)	80 (94.1)	NE (NE, NE)	0.7071 (0.2338, 2.1379) 0.5392	0.5382	
Non-White	196	20 (10.2)	176 (89.8)	NE (24.8, NE)	86	7 (8.1)	79 (91.9)	NE (NE, NE)	1.0160 (0.4247, 2.4306) 0.9716	0.9752	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.7422
Asia	147	15 (10.2)	132 (89.8)	NE (24.8, NE)	63	6 (9.5)	57 (90.5)	NE (NE, NE)	0.8440 (0.3224, 2.2093) 0.7297	0.7235	
North America	58	7 (12.1)	51 (87.9)	NE (NE, NE)	28	4 (14.3)	24 (85.7)	NE (NE, NE)	0.6255 (0.1784, 2.1938) 0.4637	0.4586	
Europe + Israel	166	7 (4.2)	159 (95.8)	NE (NE, NE)	81	2 (2.5)	79 (97.5)	NE (NE, NE)	1.4332 (0.2941, 6.9845) 0.6560	0.6552	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.7711
0	199	11 (5.5)	188 (94.5)	NE (NE, NE)	95	5 (5.3)	90 (94.7)	NE (NE, NE)	0.7553 (0.2580, 2.2108) 0.6085	0.6063	
1	172	18 (10.5)	154 (89.5)	24.8 (NE, NE)	77	7 (9.1)	70 (90.9)	NE (NE, NE)	1.0087 (0.4175, 2.4372) 0.9846	0.9856	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.0663
0	60	7 (11.7)	53 (88.3)	NE (NE, NE)	31	3 (9.7)	28 (90.3)	NE (NE, NE)	0.9635 (0.2450, 3.7885) 0.9576	0.9511	
1	107	12 (11.2)	95 (88.8)	NE (NE, NE)	48	3 (6.3)	45 (93.8)	NE (NE, NE)	1.6049 (0.4514, 5.7064) 0.4648	0.4612	
2	114	7 (6.1)	107 (93.9)	NE (NE, NE)	50	1 (2.0)	49 (98.0)	NE (NE, NE)	2.7276 (0.3346, 22.2332) 0.3486	0.3280	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	3 (3.3)	87 (96.7)	NE (24.8, NE)	43	5 (11.6)	38 (88.4)	NE (NE, NE)	0.1802 (0.0349, 0.9298) 0.0407	0.0210	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.6252
PD	173	19 (11.0)	154 (89.0)	NE (NE, NE)	77	5 (6.5)	72 (93.5)	NE (NE, NE)	1.4033 (0.5209, 3.7804)	0.5038	
PR	48	1 (2.1)	47 (97.9)	24.8 (NE, NE)	21	1 (4.8)	20 (95.2)	NE (NE, NE)	0.0000 (0.0000, ) 0.9979	0.1061	
SD	82	9 (11.0)	73 (89.0)	NE (NE, NE)	54	4 (7.4)	50 (92.6)	NE (NE, NE)	1.2848 (0.3919, 4.2126) 0.6791	0.6788	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.8117
Yes	37	4 (10.8)	33 (89.2)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	1.2241 (0.1358, 11.0339)	0.8570	0.8522
No	334	25 (7.5)	309 (92.5)	NE (24.8, NE)	159	11 (6.9)	148 (93.1)	NE (NE, NE)	0.8585 (0.4177, 1.7646)	0.6781	0.6754

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.1912
Yes	24	3 (12.5)	21 (87.5)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9967	0.3539	
No	347	26 (7.5)	321 (92.5)	NE (24.8, NE)	165	12 (7.3)	153 (92.7)	NE (NE, NE)	0.8157 (0.4070, 1.6346) 0.5657	0.5631	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.6621
Normal Function	201	14 (7.0)	187 (93.0)	NE (NE, NE)	80	4 (5.0)	76 (95.0)	NE (NE, NE)	1.0510 (0.3411, 3.2378) 0.9310	0.9311	
Mild Impairment	123	12 (9.8)	111 (90.2)	24.8 (24.8, NE)	65	4 (6.2)	61 (93.8)	NE (NE, NE)	1.3815 (0.4391, 4.3459) 0.5805	0.5848	
Moderate Impairment	41	3 (7.3)	38 (92.7)	NE (NE, NE)	23	3 (13.0)	20 (87.0)	NE (NE, NE)	0.5322 (0.1071, 2.6445) 0.4407	0.4332	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.5617
Normal Function	170	13 (7.6)	157 (92.4)	NE (24.8, NE)	88	7 (8.0)	81 (92.0)	NE (NE, NE)	0.7269 (0.2835, 1.8637) 0.5067	0.5035	
Mild Impairment	194	16 (8.2)	178 (91.8)	NE (NE, NE)	82	5 (6.1)	77 (93.9)	NE (NE, NE)	1.1367 (0.4135, 3.1251) 0.8039	0.8037	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.2359
Yes	331	25 (7.6)	306 (92.4)	NE (24.8, NE)	146	8 (5.5)	138 (94.5)	NE (NE, NE)	1.1063 (0.4941, 2.4766) 0.8060	0.8061	
No	40	4 (10.0)	36 (90.0)	NE (NE, NE)	26	4 (15.4)	22 (84.6)	NE (NE, NE)	0.5256 (0.1299, 2.1257) 0.3669	0.3555	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.5898
Positive	329	24 (7.3)	305 (92.7)	NE (24.8, NE)	152	9 (5.9)	143 (94.1)	NE (NE, NE)	1.0100 (0.4651, 2.1931) 0.9800	0.9811	
Negative	42	5 (11.9)	37 (88.1)	NE (NE, NE)	20	3 (15.0)	17 (85.0)	NE (NE, NE)	0.5169 (0.1134, 2.3568) 0.3939	0.3861	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.6283
Positive	331	23 (6.9)	308 (93.1)	NE (24.8, NE)	155	9 (5.8)	146 (94.2)	NE (NE, NE)	0.9823 (0.4500, 2.1443)	0.9643	0.9630
Negative	40	6 (15.0)	34 (85.0)	NE (NE, NE)	17	3 (17.6)	14 (82.4)	NE (2.2, NE)	0.5448 (0.1272, 2.3333)	0.4132	0.4064

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Investigations; PT: Blood bilirubin increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.4860
HER2 IHC 1+	214	15 (7.0)	199 (93.0)	NE (NE, NE)	100	5 (5.0)	95 (95.0)	NE (NE, NE)	0.8331 (0.2916, 2.3798) 0.7331	0.7313	
HER2 IHC 2+/ISH Negative	157	11 (7.0)	146 (93.0)	NE (NE, NE)	72	2 (2.8)	70 (97.2)	NE (NE, NE)	1.4431 (0.3139, 6.6350) 0.6375	0.6353	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting									0.9722
1	220	12 (5.5)	208 (94.5) NE (NE, NE)	94	3 (3.2)	91 (96.8) NE (NE, NE)	1.0863 (0.3004, 3.9280) 0.8995	0.8996	
>=2	150	14 (9.3)	136 (90.7) NE (NE, NE)	78	4 (5.1)	74 (94.9) NE (NE, NE)	1.0322 (0.3286, 3.2421) 0.9567	0.9571	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.4032
Yes	233	13 (5.6)	220 (94.4)	NE (NE, NE)	112	5 (4.5)	107 (95.5)	NE (NE, NE)	0.8081 (0.2792, 2.3385) 0.6943	0.6936	
No	98	11 (11.2)	87 (88.8)	NE (NE, NE)	43	2 (4.7)	41 (95.3)	NE (NE, NE)	1.4310 (0.3112, 6.5794) 0.6452	0.6432	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8933
<65	289	20 (6.9)	269 (93.1)	NE (NE, NE)	126	5 (4.0)	121 (96.0)	NE (NE, NE)	1.0276 (0.3769, 2.8018) 0.9575	0.9574	
>=65	82	6 (7.3)	76 (92.7)	NE (NE, NE)	46	2 (4.3)	44 (95.7)	NE (NE, NE)	1.1292 (0.2228, 5.7226) 0.8834	0.8854	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2054
<75	357	25 (7.0)	332 (93.0)	NE (NE, NE)	163	5 (3.1)	158 (96.9)	NE (NE, NE)	1.3835 (0.5195, 3.6842) 0.5160	0.5141	
>=75	14	1 (7.1)	13 (92.9)	NE (6.2, NE)	9	2 (22.2)	7 (77.8)	NE (3.7, NE)	0.3022 (0.0274, 3.3354) 0.3287	0.3001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.2883
White	175	9 (5.1)	166 (94.9)	NE (NE, NE)	85	4 (4.7)	81 (95.3)	NE (NE, NE)	0.7198 (0.2131, 2.4313) 0.5966	0.5948	
Non-White	196	17 (8.7)	179 (91.3)	NE (NE, NE)	86	3 (3.5)	83 (96.5)	NE (NE, NE)	1.4220 (0.4096, 4.9375) 0.5793	0.5776	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood bilirubin increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.3101
Asia	147	13 (8.8)	134 (91.2)	NE (NE, NE)	63	3 (4.8)	60 (95.2)	NE (NE, NE)	1.0213 (0.2838, 3.6754) 0.9743	0.9748	
North America	58	4 (6.9)	54 (93.1)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9959	0.2294	
Europe + Israel	166	9 (5.4)	157 (94.6)	NE (NE, NE)	81	4 (4.9)	77 (95.1)	NE (NE, NE)	0.6608 (0.1962, 2.2256) 0.5037	0.5014	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood bilirubin increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.9069
0	199	12 (6.0)	187 (94.0)	NE (NE, NE)	95	3 (3.2)	92 (96.8)	NE (NE, NE)	1.0982 (0.3003, 4.0164) 0.8874	0.8872	
1	172	14 (8.1)	158 (91.9)	NE (NE, NE)	77	4 (5.2)	73 (94.8)	NE (NE, NE)	0.9649 (0.3087, 3.0161) 0.9509	0.9514	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood bilirubin increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.9875
0	60	6 (10.0)	54 (90.0)	NE (18.6, NE)	31	2 (6.5)	29 (93.5)	NE (NE, NE)	0.7608 (0.1420, 4.0755) 0.7496	0.7489	
1	107	6 (5.6)	101 (94.4)	NE (NE, NE)	48	2 (4.2)	46 (95.8)	NE (NE, NE)	1.0175 (0.2032, 5.0957) 0.9832	0.9844	
2	114	8 (7.0)	106 (93.0)	NE (NE, NE)	50	2 (4.0)	48 (96.0)	NE (NE, NE)	1.2798 (0.2677, 6.1186) 0.7573	0.7567	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood bilirubin increased

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	6 (6.7)	84 (93.3) NE (NE, NE)	43	1 (2.3)	42 (97.7) NE (NE, NE)	1.0585 (0.1171, 9.5695) 0.9597	0.9597	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood bilirubin increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.1612
PD	173	13 (7.5)	160 (92.5)	NE (NE, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	1.7674 (0.3895, 8.0192) 0.4604	0.4548	
PR	48	3 (6.3)	45 (93.8)	NE (NE, NE)	21	3 (14.3)	18 (85.7)	NE (NE, NE)	0.1986 (0.0313, 1.2595) 0.0863	0.0591	
SD	82	3 (3.7)	79 (96.3)	NE (NE, NE)	54	2 (3.7)	52 (96.3)	NE (NE, NE)	0.7428 (0.1211, 4.5541) 0.7479	0.7471	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood bilirubin increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.6625
Yes	37	3 (8.1)	34 (91.9)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	0.8524 (0.0875, 8.3080)	0.8907	0.8906
No	334	23 (6.9)	311 (93.1)	NE (NE, NE)	159	6 (3.8)	153 (96.2)	NE (NE, NE)	1.0253 (0.4078, 2.5781)	0.9576	0.9575

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Blood bilirubin increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.2909
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	1 (14.3)	6 (85.7)	NE (1.4, NE)	0.3015 (0.0188, 4.8253) 0.3967	0.3686	
No	347	25 (7.2)	322 (92.8)	NE (NE, NE)	165	6 (3.6)	159 (96.4)	NE (NE, NE)	1.1295 (0.4535, 2.8133) 0.7936	0.7941	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Blood bilirubin increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.6023
Normal Function	201	12 (6.0)	189 (94.0)	NE (NE, NE)	80	4 (5.0)	76 (95.0)	NE (NE, NE)	0.6703 (0.2089, 2.1511) 0.5013	0.4988	
Mild Impairment	123	10 (8.1)	113 (91.9)	NE (NE, NE)	65	2 (3.1)	63 (96.9)	NE (NE, NE)	1.7714 (0.3767, 8.3307) 0.4692	0.4638	
Moderate Impairment	41	4 (9.8)	37 (90.2)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	1.7532 (0.1951, 15.7581) 0.6163	0.6117	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Investigations; PT: Blood bilirubin increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.4073
Normal Function	170	6 (3.5)	164 (96.5)	NE (NE, NE)	88	1 (1.1)	87 (98.9)	NE (NE, NE)	1.5533 (0.1795, 13.4417) 0.6892	0.6870	
Mild Impairment	194	18 (9.3)	176 (90.7)	NE (NE, NE)	82	6 (7.3)	76 (92.7)	NE (NE, NE)	0.7075 (0.2732, 1.8320) 0.4759	0.4735	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood bilirubin increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.3178
Yes	331	24 (7.3)	307 (92.7)	NE (NE, NE)	146	7 (4.8)	139 (95.2)	NE (NE, NE)	0.9923 (0.4220, 2.3334) 0.9859	0.9852	
No	40	2 (5.0)	38 (95.0)	NE (18.6, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.8383	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood bilirubin increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.3135
Positive	329	24 (7.3)	305 (92.7)	NE (NE, NE)	152	7 (4.6)	145 (95.4)	NE (NE, NE)	0.9407 (0.3970, 2.2290) 0.8896	0.8887	
Negative	42	2 (4.8)	40 (95.2)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) 0.9973	0.4243	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood bilirubin increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.3524
Positive	331	24 (7.3)	307 (92.7)	NE (NE, NE)	155	7 (4.5)	148 (95.5)	NE (NE, NE)	0.9554 (0.4031, 2.2644)	0.9175	
Negative	40	2 (5.0)	38 (95.0)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) 0.9975	0.4730	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Gamma-glutamyltransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.4414
HER2 IHC 1+	214	12 (5.6)	202 (94.4)	NE (NE, NE)	100	6 (6.0)	94 (94.0)	NE (NE, NE)	0.8006 (0.2975, 2.1546) 0.6597	0.6577	
HER2 IHC 2+/ISH Negative	157	8 (5.1)	149 (94.9)	NE (NE, NE)	72	2 (2.8)	70 (97.2)	NE (13.6, NE)	1.2121 (0.2502, 5.8708) 0.8112	0.8115	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Gamma-glutamyltransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.5632
1	220	13 (5.9)	207 (94.1)	NE (NE, NE)	94	4 (4.3)	90 (95.7)	NE (NE, NE)	1.1582 (0.3731, 3.5956) 0.7994	0.8029	
>=2	150	7 (4.7)	143 (95.3)	NE (NE, NE)	78	4 (5.1)	74 (94.9)	NE (13.6, NE)	0.6189 (0.1754, 2.1837) 0.4557	0.4520	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Gamma-glutamyltransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.1067
Yes	233	13 (5.6)	220 (94.4)	NE (NE, NE)	112	3 (2.7)	109 (97.3)	NE (NE, NE)	1.6513 (0.4629, 5.8906) 0.4395	0.4361	
No	98	6 (6.1)	92 (93.9)	NE (NE, NE)	43	5 (11.6)	38 (88.4)	NE (13.6, NE)	0.3985 (0.1199, 1.3242) 0.1332	0.1205	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Gamma-glutamyltransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2676
<65	289	15 (5.2)	274 (94.8)	NE (NE, NE)	126	7 (5.6)	119 (94.4)	NE (13.6, NE)	0.6562 (0.2607, 1.6514) 0.3710	0.3671	
>=65	82	5 (6.1)	77 (93.9)	NE (NE, NE)	46	1 (2.2)	45 (97.8)	NE (NE, NE)	2.7990 (0.3270, 23.9588) 0.3475	0.3267	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Gamma-glutamyltransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2876
<75	357	19 (5.3)	338 (94.7)	NE (NE, NE)	163	8 (4.9)	155 (95.1)	NE (13.6, NE)	0.8183 (0.3516, 1.9043) 0.6417	0.6389	
>=75	14	1 (7.1)	13 (92.9)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9985	0.4142	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Investigations; PT: Gamma-glutamyltransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.4808
White	175	10 (5.7)	165 (94.3)	NE (NE, NE)	85	3 (3.5)	82 (96.5)	NE (13.6, NE)	1.0945 (0.2911, 4.1148) 0.8936	0.8936	
Non-White	196	10 (5.1)	186 (94.9)	NE (NE, NE)	86	5 (5.8)	81 (94.2)	NE (NE, NE)	0.7425 (0.2509, 2.1971) 0.5907	0.5861	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Gamma-glutamyltransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.5844
Asia	147	9 (6.1)	138 (93.9)	NE (NE, NE)	63	5 (7.9)	58 (92.1)	NE (NE, NE)	0.6439 (0.2129, 1.9476) 0.4357	0.4279	
North America	58	0	58 (100)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) NE		
Europe + Israel	166	11 (6.6)	155 (93.4)	NE (NE, NE)	81	3 (3.7)	78 (96.3)	NE (13.6, NE)	1.2907 (0.3510, 4.7461) 0.7009	0.7001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Investigations; PT: Gamma-glutamyltransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.0264
0	199	9 (4.5)	190 (95.5)	NE (NE, NE)	95	7 (7.4)	88 (92.6)	NE (13.6, NE)	0.4265 (0.1539, 1.1820) 0.1013	0.0922	
1	172	11 (6.4)	161 (93.6)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	4.1970 (0.5380, 32.7410) 0.1711	0.1371	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Gamma-glutamyltransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.9329
0	60	4 (6.7)	56 (93.3)	NE (NE, NE)	31	2 (6.5)	29 (93.5)	NE (NE, NE)	0.6626 (0.1131, 3.8809) 0.6482	0.6462	
1	107	5 (4.7)	102 (95.3)	NE (NE, NE)	48	3 (6.3)	45 (93.8)	NE (13.6, NE)	0.5575 (0.1284, 2.4205) 0.4354	0.4281	
2	114	4 (3.5)	110 (96.5)	NE (NE, NE)	50	1 (2.0)	49 (98.0)	NE (NE, NE)	1.6246 (0.1809, 14.5872) 0.6648	0.6617	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Gamma-glutamyltransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	7 (7.8)	83 (92.2)	NE (NE, NE)	43	2 (4.7)	41 (95.3)	NE (NE, NE)	1.3303 (0.2717, 6.5145) 0.7247	0.7249	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Gamma-glutamyltransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.6028
PD	173	9 (5.2)	164 (94.8)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	3.0963 (0.3881, 24.7037)	0.2614	
PR	48	2 (4.2)	46 (95.8)	NE (NE, NE)	21	1 (4.8)	20 (95.2)	NE (NE, NE)	0.2861 (0.0797, 9.6980)	0.9113	
SD	82	5 (6.1)	77 (93.9)	NE (NE, NE)	54	1 (1.9)	53 (98.1)	NE (NE, NE)	0.8794 (0.3276, 24.4909)	0.3230	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Gamma-glutamyltransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											1.0000
Yes	37	0	37 (100)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE)		
No	334	20 (6.0)	314 (94.0)	NE (NE, NE)	159	8 (5.0)	151 (95.0)	NE (NE, NE)	0.9150 (0.3968, 2.1099)	0.8324	0.8349

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Gamma-glutamyltransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.4707
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.5812	
No	347	19 (5.5)	328 (94.5)	NE (NE, NE)	165	8 (4.8)	157 (95.2)	NE (NE, NE)	0.8508 (0.3660, 1.9779) 0.7074	0.7047	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Gamma-glutamyltransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.7247
Normal Function	201	11 (5.5)	190 (94.5)	NE (NE, NE)	80	5 (6.3)	75 (93.8)	NE (NE, NE)	0.7569 (0.2588, 2.2133) 0.6109	0.6067	
Mild Impairment	123	6 (4.9)	117 (95.1)	NE (NE, NE)	65	2 (3.1)	63 (96.9)	NE (NE, NE)	0.9852 (0.1913, 5.0739) 0.9858	0.9858	
Moderate Impairment	41	3 (7.3)	38 (92.7)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (13.6, NE)	1.6190 (0.1684, 15.5652) 0.6765	0.6733	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Gamma-glutamyltransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.6373
Normal Function	170	11 (6.5)	159 (93.5)	NE (NE, NE)	88	4 (4.5)	84 (95.5)	NE (13.6, NE)	1.0613 (0.3311, 3.4016) 0.9203	0.9220	
Mild Impairment	194	9 (4.6)	185 (95.4)	NE (NE, NE)	82	4 (4.9)	78 (95.1)	NE (NE, NE)	0.7491 (0.2251, 2.4924) 0.6376	0.6359	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Gamma-glutamyltransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.4930
Yes	331	16 (4.8)	315 (95.2)	NE (NE, NE)	146	7 (4.8)	139 (95.2)	NE (NE, NE)	0.8318 (0.3381, 2.0463) 0.6884	0.6853	
No	40	4 (10.0)	36 (90.0)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	1.0142 (0.0931, 11.0446) 0.9908	0.9907	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Gamma-glutamyltransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.3911
Positive	329	19 (5.8)	310 (94.2)	NE (NE, NE)	152	8 (5.3)	144 (94.7)	NE (NE, NE)	0.8327 (0.3590, 1.9314)	0.6669	
Negative	42	1 (2.4)	41 (97.6)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) 0.9978	0.4902	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Gamma-glutamyltransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.4169
Positive	331	19 (5.7)	312 (94.3)	NE (NE, NE)	155	8 (5.2)	147 (94.8)	NE (NE, NE)	0.8440 (0.3638, 1.9583)	0.6901	
Negative	40	1 (2.5)	39 (97.5)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) 0.9978	0.5145	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood lactate dehydrogenase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.1947
HER2 IHC 1+	214	10 (4.7)	204 (95.3)	NE (NE, NE)	100	7 (7.0)	93 (93.0)	NE (NE, NE)	0.4647 (0.1720, 1.2551) 0.1306	0.1223	
HER2 IHC 2+/ISH Negative	157	9 (5.7)	148 (94.3)	NE (NE, NE)	72	2 (2.8)	70 (97.2)	NE (NE, NE)	1.4749 (0.3124, 6.9638) 0.6236	0.6212	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood lactate dehydrogenase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.2563
1	220	15 (6.8)	205 (93.2)	NE (NE, NE)	94	5 (5.3)	89 (94.7)	NE (NE, NE)	0.9929 (0.3562, 2.7677) 0.9892	0.9924	
>=2	150	4 (2.7)	146 (97.3)	NE (NE, NE)	78	4 (5.1)	74 (94.9)	NE (NE, NE)	0.2881 (0.0687, 1.2080) 0.0888	0.0718	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: Blood lactate dehydrogenase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.7414
Yes	233	10 (4.3)	223 (95.7)	NE (NE, NE)	112	5 (4.5)	107 (95.5)	NE (NE, NE)	0.6482 (0.2125, 1.9769) 0.4460	0.4437	
No	98	8 (8.2)	90 (91.8)	NE (NE, NE)	43	3 (7.0)	40 (93.0)	NE (NE, NE)	0.9024 (0.2371, 3.4342) 0.8803	0.8803	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.8.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Investigations; PT: Blood lactate dehydrogenase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1703
<65	289	14 (4.8)	275 (95.2)	NE (NE, NE)	126	8 (6.3)	118 (93.7)	NE (NE, NE)	0.5003 (0.2046, 1.2233) 0.1290	0.1225	
>=65	82	5 (6.1)	77 (93.9)	NE (NE, NE)	46	1 (2.2)	45 (97.8)	NE (NE, NE)	2.4603 (0.2846, 21.2717) 0.4134	0.3979	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: Blood lactate dehydrogenase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2005
<75	357	19 (5.3)	338 (94.7)	NE (NE, NE)	163	8 (4.9)	155 (95.1)	NE (NE, NE)	0.7598 (0.3264, 1.7685) 0.5239	0.5237	
>=75	14	0	14 (100)	NE (NE, NE)	9	1 (11.1)	8 (88.9)	NE (3.0, NE)	0.0000 (0.0000, ) 0.9984	0.2207	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood lactate dehydrogenase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.2788
White	175	10 (5.7)	165 (94.3)	NE (NE, NE)	85	3 (3.5)	82 (96.5)	NE (NE, NE)	1.1107 (0.2970, 4.1535) 0.8760	0.8755	
Non-White	196	9 (4.6)	187 (95.4)	NE (NE, NE)	86	6 (7.0)	80 (93.0)	NE (NE, NE)	0.4867 (0.1705, 1.3898) 0.1786	0.1703	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood lactate dehydrogenase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.6252
Asia	147	8 (5.4)	139 (94.6)	NE (NE, NE)	63	5 (7.9)	58 (92.1)	NE (NE, NE)	0.4851 (0.1550, 1.5174) 0.2138	0.2053	
North America	58	2 (3.4)	56 (96.6)	NE (16.6, NE)	28	1 (3.6)	27 (96.4)	NE (NE, NE)	0.2810 (0.0174, 4.5378) 0.3711	0.3398	
Europe + Israel	166	9 (5.4)	157 (94.6)	NE (NE, NE)	81	3 (3.7)	78 (96.3)	NE (NE, NE)	1.1656 (0.3101, 4.3811) 0.8205	0.8200	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood lactate dehydrogenase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.8560
0	199	10 (5.0)	189 (95.0)	NE (NE, NE)	95	5 (5.3)	90 (94.7)	NE (NE, NE)	0.6633 (0.2223, 1.9789) 0.4616	0.4599	
1	172	9 (5.2)	163 (94.8)	NE (NE, NE)	77	4 (5.2)	73 (94.8)	NE (NE, NE)	0.7461 (0.2247, 2.4774) 0.6324	0.6306	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood lactate dehydrogenase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.3773
0	60	4 (6.7)	56 (93.3)	NE (NE, NE)	31	2 (6.5)	29 (93.5)	NE (NE, NE)	0.7294 (0.1304, 4.0800) 0.7194	0.7184	
1	107	5 (4.7)	102 (95.3)	NE (NE, NE)	48	4 (8.3)	44 (91.7)	NE (NE, NE)	0.4596 (0.1226, 1.7224) 0.2488	0.2372	
2	114	8 (7.0)	106 (93.0)	NE (NE, NE)	50	1 (2.0)	49 (98.0)	NE (NE, NE)	2.2861 (0.2744, 19.0480) 0.4447	0.4326	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood lactate dehydrogenase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	2 (2.2)	88 (97.8)	NE (NE, NE)	43	2 (4.7)	41 (95.3)	NE (NE, NE)	0.3577 (0.0480, 2.6652) 0.3157	0.2987	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood lactate dehydrogenase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.5959
PD	173	4 (2.3)	169 (97.7)	NE (NE, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	0.4561 (0.0995, 2.0906)	0.3005	
PR	48	1 (2.1)	47 (97.9)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	0.3122 (NE, NE)	0.6678	
SD	82	7 (8.5)	75 (91.5)	NE (NE, NE)	54	5 (9.3)	49 (90.7)	NE (NE, NE)	0.9984 (0.2041, 2.1225)	0.4824	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: Blood lactate dehydrogenase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.4504
Yes	37	1 (2.7)	36 (97.3)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	0.2325 (0.0137, 3.9440)	0.2743	
No	334	18 (5.4)	316 (94.6)	NE (NE, NE)	159	8 (5.0)	151 (95.0)	NE (NE, NE)	0.3125 (0.3250, 1.7833)	0.5289	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood lactate dehydrogenase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.7948
Yes	24	2 (8.3)	22 (91.7)	NE (NE, NE)	7	1 (14.3)	6 (85.7)	NE (0.3, NE)	0.5520 (0.0499, 6.1075) 0.6280	0.6230	
No	347	17 (4.9)	330 (95.1)	NE (NE, NE)	165	8 (4.8)	157 (95.2)	NE (NE, NE)	0.6952 (0.2939, 1.6440) 0.4077	0.4057	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood lactate dehydrogenase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.4669
Normal Function	201	11 (5.5)	190 (94.5)	NE (NE, NE)	80	6 (7.5)	74 (92.5)	NE (NE, NE)	0.4784 (0.1701, 1.3455) 0.1623	0.1541	
Mild Impairment	123	7 (5.7)	116 (94.3)	NE (NE, NE)	65	3 (4.6)	62 (95.4)	NE (NE, NE)	0.9136 (0.2309, 3.6141) 0.8975	0.8963	
Moderate Impairment	41	1 (2.4)	40 (97.6)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9979	0.5308	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: Blood lactate dehydrogenase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.5453
Normal Function	170	9 (5.3)	161 (94.7)	NE (NE, NE)	88	6 (6.8)	82 (93.2)	NE (NE, NE)	0.4515 (0.1558, 1.3084) 0.1430	0.1344	
Mild Impairment	194	9 (4.6)	185 (95.4)	NE (NE, NE)	82	3 (3.7)	79 (96.3)	NE (NE, NE)	1.0952 (0.2947, 4.0697) 0.8920	0.8919	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: Blood lactate dehydrogenase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.8883
Yes	331	15 (4.5)	316 (95.5)	NE (NE, NE)	146	7 (4.8)	139 (95.2)	NE (NE, NE)	0.6762 (0.2705, 1.6904) 0.4026	0.4012	
No	40	4 (10.0)	36 (90.0)	NE (NE, NE)	26	2 (7.7)	24 (92.3)	NE (NE, NE)	0.8357 (0.1473, 4.7409) 0.8394	0.8392	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood lactate dehydrogenase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.1845
Positive	329	18 (5.5)	311 (94.5)	NE (NE, NE)	152	7 (4.6)	145 (95.4)	NE (NE, NE)	0.8529 (0.3506, 2.0750)	0.7268	
Negative	42	1 (2.4)	41 (97.6)	NE (NE, NE)	20	2 (10.0)	18 (90.0)	NE (3.7, NE)	0.1718 (0.0151, 1.9504)	0.1099	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: Blood lactate dehydrogenase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.4980
Positive	331	18 (5.4)	313 (94.6)	NE (NE, NE)	155	8 (5.2)	147 (94.8)	NE (NE, NE)	0.7513 (0.3214, 1.7562)	0.5089	
Negative	40	1 (2.5)	39 (97.5)	NE (NE, NE)	17	1 (5.9)	16 (94.1)	NE (3.0, NE)	0.3616 (0.0223, 5.8518)	0.4553	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Ejection fraction decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.9999
HER2 IHC 1+	214	10 (4.7)	204 (95.3)	NE (NE, NE)	100	0	100 (100)	NE (NE, NE)	NE (NE, NE) 0.9918	0.1516	
HER2 IHC 2+/ISH Negative	157	6 (3.8)	151 (96.2)	NE (NE, NE)	72	0	72 (100)	NE (NE, NE)	NE (NE, NE) 0.9954	0.1842	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: Ejection fraction decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.9997
1	220	13 (5.9)	207 (94.1)	NE (NE, NE)	94	0	94 (100)	NE (NE, NE)	NE (NE, NE) 0.9937	0.0835	
>=2	150	3 (2.0)	147 (98.0)	NE (NE, NE)	78	0	78 (100)	NE (NE, NE)	NE (NE, NE) 0.9967	0.3504	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Ejection fraction decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.9997
Yes	233	10 (4.3)	223 (95.7)	NE (NE, NE)	112	0	112 (100)	NE (NE, NE)	NE (NE, NE) 0.9918	0.1448	
No	98	2 (2.0)	96 (98.0)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9975	0.4924	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.8.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Investigations; PT: Ejection fraction decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9999
<65	289	13 (4.5)	276 (95.5)	NE (NE, NE)	126	0	126 (100)	NE (NE, NE)	NE (NE, NE) 0.9906	0.0996	
>=65	82	3 (3.7)	79 (96.3)	NE (NE, NE)	46	0	46 (100)	NE (NE, NE)	NE (NE, NE) 0.9967	0.3457	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Ejection fraction decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9998
<75	357	15 (4.2)	342 (95.8)	NE (NE, NE)	163	0	163 (100)	NE (NE, NE)	NE (NE, NE) 0.9896	0.0627	
>=75	14	1 (7.1)	13 (92.9)	NE (8.4, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9985	0.4795	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Ejection fraction decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.9999
White	175	8 (4.6)	167 (95.4)	NE (NE, NE)	85	0	85 (100)	NE (NE, NE)	NE (NE, NE) 0.9929	0.2136	
Non-White	196	8 (4.1)	188 (95.9)	NE (NE, NE)	86	0	86 (100)	NE (NE, NE)	NE (NE, NE) 0.9947	0.1373	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Ejection fraction decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											1.0000
Asia	147	3 (2.0)	144 (98.0)	NE (NE, NE)	63	0	63 (100)	NE (NE, NE)	NE (NE, NE) 0.9966	0.3283	
North America	58	4 (6.9)	54 (93.1)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9958	0.4613	
Europe + Israel	166	9 (5.4)	157 (94.6)	NE (NE, NE)	81	0	81 (100)	NE (NE, NE)	NE (NE, NE) 0.9946	0.1310	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Ejection fraction decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.9999
0	199	8 (4.0)	191 (96.0)	NE (NE, NE)	95	0	95 (100)	NE (NE, NE)	NE (NE, NE) 0.9950	0.1761	
1	172	8 (4.7)	164 (95.3)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE) 0.9951	0.1614	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Ejection fraction decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											1.0000
0	60	4 (6.7)	56 (93.3)	NE (NE, NE)	31	0	31 (100)	NE (NE, NE)	NE (NE, NE) 0.9960	0.2403	
1	107	3 (2.8)	104 (97.2)	NE (NE, NE)	48	0	48 (100)	NE (NE, NE)	NE (NE, NE) 0.9967	0.3557	
2	114	5 (4.4)	109 (95.6)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	NE (NE, NE) 0.9955	0.4447	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: Ejection fraction decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	4 (4.4)	86 (95.6)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9965	0.3416	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Ejection fraction decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											1.0000
PD	173	6 (3.5)	167 (96.5)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE) 0.9944	0.3353	
PR	48	5 (10.4)	43 (89.6)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	NE (NE, NE) 0.9963	0.3163	
SD	82	2 (2.4)	80 (97.6)	NE (NE, NE)	54	0	54 (100)	NE (NE, NE)	NE (NE, NE) 0.9967	0.2926	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Ejection fraction decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.9999
Yes	37	1 (2.7)	36 (97.3)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9982	0.7728	
No	334	15 (4.5)	319 (95.5)	NE (NE, NE)	159	0	159 (100)	NE (NE, NE)	NE (NE, NE) 0.9892	0.0504	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.8.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Investigations; PT: Ejection fraction decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											1.0000
Yes	24	1 (4.2)	23 (95.8)	NE (10.8, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9987	0.7389	
No	347	15 (4.3)	332 (95.7)	NE (NE, NE)	165	0	165 (100)	NE (NE, NE)	NE (NE, NE) 0.9893	0.0534	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Ejection fraction decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											1.0000
Normal Function	201	8 (4.0)	193 (96.0)	NE (NE, NE)	80	0	80 (100)	NE (NE, NE)	NE (NE, NE) 0.9934	0.2516	
Mild Impairment	123	5 (4.1)	118 (95.9)	NE (NE, NE)	65	0	65 (100)	NE (NE, NE)	NE (NE, NE) 0.9956	0.2085	
Moderate Impairment	41	2 (4.9)	39 (95.1)	NE (15.2, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9969	0.3462	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Investigations; PT: Ejection fraction decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.9999
Normal Function	170	9 (5.3)	161 (94.7)	NE (NE, NE)	88	0	88 (100)	NE (NE, NE)	NE (NE, NE) 0.9943	0.1026	
Mild Impairment	194	7 (3.6)	187 (96.4)	NE (NE, NE)	82	0	82 (100)	NE (NE, NE)	NE (NE, NE) 0.9935	0.2600	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Investigations; PT: Ejection fraction decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.9999
Yes	331	15 (4.5)	316 (95.5)	NE (NE, NE)	146	0	146 (100)	NE (NE, NE)	NE (NE, NE) 0.9893	0.0557	
No	40	1 (2.5)	39 (97.5)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9984	0.7995	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Investigations; PT: Ejection fraction decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.9994
Positive	329	12 (3.6)	317 (96.4)	NE (NE, NE)	152	0	152 (100)	NE (NE, NE)	NE (NE, NE) 0.9907	0.0977	
Negative	42	4 (9.5)	38 (90.5)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) 0.9966	0.3199	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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SOC: Investigations; PT: Ejection fraction decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.9994
Positive	331	12 (3.6)	319 (96.4)	NE (NE, NE)	155	0	155 (100)	NE (NE, NE)	NE (NE, NE) 0.9906	0.0950	
Negative	40	4 (10.0)	36 (90.0)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) 0.9968	0.3551	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Investigations; PT: Blood creatinine increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.9980
HER2 IHC 1+	214	8 (3.7)	206 (96.3)	NE (NE, NE)	100	4 (4.0)	96 (96.0)	NE (12.1, NE)	0.6928 (0.2017, 2.3804) 0.5601	0.5567	
HER2 IHC 2+/ISH Negative	157	6 (3.8)	151 (96.2)	NE (NE, NE)	72	3 (4.2)	69 (95.8)	NE (14.4, NE)	0.5874 (0.1407, 2.4519) 0.4655	0.4610	

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 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Blood creatinine increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.4144
1	220	6 (2.7)	214 (97.3)	NE (NE, NE)	94	4 (4.3)	90 (95.7)	NE (12.1, NE)	0.4687 (0.1268, 1.7328) 0.2560	0.2457	
>=2	150	8 (5.3)	142 (94.7)	NE (NE, NE)	78	3 (3.8)	75 (96.2)	NE (14.4, NE)	0.8966 (0.2289, 3.5116) 0.8755	0.8737	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Investigations; PT: Blood creatinine increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.0219
Yes	233	11 (4.7)	222 (95.3)	NE (NE, NE)	112	2 (1.8)	110 (98.2)	NE (NE, NE)	2.1900 (0.4792, 10.0095) 0.3120	0.2995	
No	98	2 (2.0)	96 (98.0)	NE (NE, NE)	43	4 (9.3)	39 (90.7)	NE (12.1, NE)	0.0966 (0.0170, 0.5499) 0.0084	0.0015	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Investigations; PT: Blood creatinine increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1227
<65	289	10 (3.5)	279 (96.5)	NE (NE, NE)	126	2 (1.6)	124 (98.4)	NE (NE, NE)	1.7755 (0.3833, 8.2240) 0.4629	0.4580	
>=65	82	4 (4.9)	78 (95.1)	NE (NE, NE)	46	5 (10.9)	41 (89.1)	14.4 (12.1, NE)	0.2573 (0.0647, 1.0226) 0.0538	0.0406	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4561
<75	357	12 (3.4)	345 (96.6)	NE (NE, NE)	163	4 (2.5)	159 (97.5)	NE (NE, NE)	1.0166 (0.3199, 3.2312) 0.9777	0.9786	
>=75	14	2 (14.3)	12 (85.7)	NE (3.9, NE)	9	3 (33.3)	6 (66.7)	14.4 (0.3, 14.4)	0.4067 (0.0661, 2.5009) 0.3316	0.3167	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood creatinine increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.9662
White	175	8 (4.6)	167 (95.4)	NE (NE, NE)	85	4 (4.7)	81 (95.3)	NE (12.1, NE)	0.7310 (0.2138, 2.4991) 0.6173	0.6161	
Non-White	196	6 (3.1)	190 (96.9)	NE (NE, NE)	86	3 (3.5)	83 (96.5)	NE (14.4, NE)	0.5398 (0.1276, 2.2827) 0.4020	0.3954	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood creatinine increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.8966
Asia	147	5 (3.4)	142 (96.6)	NE (NE, NE)	63	3 (4.8)	60 (95.2)	NE (14.4, NE)	0.4086 (0.0910, 1.8345) 0.2428	0.2296	
North America	58	4 (6.9)	54 (93.1)	NE (NE, NE)	28	2 (7.1)	26 (92.9)	NE (NE, NE)	0.8901 (0.1625, 4.8753) 0.8933	0.9010	
Europe + Israel	166	5 (3.0)	161 (97.0)	NE (NE, NE)	81	2 (2.5)	79 (97.5)	NE (12.1, NE)	0.8066 (0.1495, 4.3505) 0.8026	0.8023	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood creatinine increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.9739
0	199	8 (4.0)	191 (96.0)	NE (NE, NE)	95	4 (4.2)	91 (95.8)	NE (12.1, NE)	0.5897 (0.1707, 2.0366) 0.4036	0.3981	
1	172	6 (3.5)	166 (96.5)	NE (NE, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	0.6925 (0.1658, 2.8921) 0.6144	0.6142	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Blood creatinine increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.8894
0	60	1 (1.7)	59 (98.3)	NE (NE, NE)	31	1 (3.2)	30 (96.8)	NE (NE, NE)	0.5210 (0.0326, 8.3303) 0.6448	0.6389	
1	107	3 (2.8)	104 (97.2)	NE (NE, NE)	48	2 (4.2)	46 (95.8)	NE (12.1, NE)	0.4819 (0.0787, 2.9522) 0.4299	0.4181	
2	114	7 (6.1)	107 (93.9)	NE (NE, NE)	50	2 (4.0)	48 (96.0)	NE (NE, NE)	1.1982 (0.2421, 5.9291) 0.8246	0.8236	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood creatinine increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	3 (3.3)	87 (96.7)	NE (NE, NE)	43	2 (4.7)	41 (95.3)	14.4 (14.4, NE)	0.3285 (0.0484, 2.2285) 0.2544	0.2357	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood creatinine increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.1080
PD	173	9 (5.2)	164 (94.8)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	3.5306 (0.4453, 27.9930)	0.2018	
PR	48	0	48 (100)	NE (NE, NE)	21	1 (4.8)	20 (95.2)	NE (NE, NE)	0.2324 (0.0000, )	0.1306	
SD	82	3 (3.7)	79 (96.3)	NE (NE, NE)	54	2 (3.7)	52 (96.3)	NE (12.1, NE)	0.8298 (0.1344, 5.1233)	0.8387	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood creatinine increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.0969
Yes	37	0	37 (100)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	0.0000 (0.0000, ) 0.9980	0.0916	
No	334	14 (4.2)	320 (95.8)	NE (NE, NE)	159	6 (3.8)	153 (96.2)	NE (14.4, NE)	0.7610 (0.2839, 2.0399) 0.5872	0.5847	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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SOC: Investigations; PT: Blood creatinine increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.9998
Yes	24	0	24 (100)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE)		
No	347	14 (4.0)	333 (96.0)	NE (NE, NE)	165	7 (4.2)	158 (95.8)	NE (14.4, NE)	0.6507 (0.2547, 1.6626) 0.3693	0.3654	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Investigations; PT: Blood creatinine increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.5186
Normal Function	201	5 (2.5)	196 (97.5)	NE (NE, NE)	80	1 (1.3)	79 (98.8)	NE (NE, NE)	1.7470 (0.2021, 15.0994) 0.6121	0.6098	
Mild Impairment	123	4 (3.3)	119 (96.7)	NE (NE, NE)	65	1 (1.5)	64 (98.5)	NE (NE, NE)	1.9228 (0.2139, 17.2800) 0.5595	0.5526	
Moderate Impairment	41	5 (12.2)	36 (87.8)	NE (NE, NE)	23	5 (21.7)	18 (78.3)	14.4 (12.1, NE)	0.4209 (0.1207, 1.4685) 0.1747	0.1636	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood creatinine increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.7435
Normal Function	170	6 (3.5)	164 (96.5)	NE (NE, NE)	88	4 (4.5)	84 (95.5)	NE (12.1, NE)	0.3475 (0.0909, 1.3284) 0.1224	0.1090	
Mild Impairment	194	7 (3.6)	187 (96.4)	NE (NE, NE)	82	3 (3.7)	79 (96.3)	NE (NE, NE)	0.8971 (0.2303, 3.4948) 0.8756	0.8746	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood creatinine increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.3244
Yes	331	13 (3.9)	318 (96.1)	NE (NE, NE)	146	7 (4.8)	139 (95.2)	NE (14.4, NE)	0.6036 (0.2354, 1.5478) 0.2933	0.2883	
No	40	1 (2.5)	39 (97.5)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9985	0.8185	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood creatinine increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.6139
Positive	329	13 (4.0)	316 (96.0)	NE (NE, NE)	152	6 (3.9)	146 (96.1)	NE (14.4, NE)	0.6746 (0.2489, 1.8282) 0.4390	0.4350	
Negative	42	1 (2.4)	41 (97.6)	NE (NE, NE)	20	1 (5.0)	19 (95.0)	NE (NE, NE)	0.4820 (0.0301, 7.7061) 0.6058	0.5978	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Blood creatinine increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.5466
Positive	331	13 (3.9)	318 (96.1)	NE (NE, NE)	155	6 (3.9)	149 (96.1)	NE (14.4, NE)	0.6832 (0.2519, 1.8526)	0.4504	
Negative	40	1 (2.5)	39 (97.5)	NE (NE, NE)	17	1 (5.9)	16 (94.1)	NE (NE, NE)	0.4305 (0.0269, 6.8829)	0.5393	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Electrocardiogram QT prolonged

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.6371
HER2 IHC 1+	214	4 (1.9)	210 (98.1)	NE (NE, NE)	100	2 (2.0)	98 (98.0)	NE (NE, NE)	0.5807 (0.0984, 3.4267) 0.5484	0.5446	
HER2 IHC 2+/ISH Negative	157	7 (4.5)	150 (95.5)	NE (NE, NE)	72	2 (2.8)	70 (97.2)	NE (NE, NE)	0.7526 (0.1500, 3.7756) 0.7298	0.7291	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Electrocardiogram QT prolonged

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.9867
1	220	3 (1.4)	217 (98.6)	NE (NE, NE)	94	1 (1.1)	93 (98.9)	NE (NE, NE)	1.1332 (0.1175, 10.9298) 0.9139	0.9139	
>=2	150	8 (5.3)	142 (94.7)	NE (NE, NE)	78	3 (3.8)	75 (96.2)	NE (7.1, NE)	0.5164 (0.1274, 2.0936) 0.3548	0.3479	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.8074
Yes	233	4 (1.7)	229 (98.3)	NE (NE, NE)	112	1 (0.9)	111 (99.1)	NE (NE, NE)	1.0527 (0.1106, 10.0166) 0.9643	0.9643	
No	98	5 (5.1)	93 (94.9)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	1.0721 (0.1224, 9.3927) 0.9498	0.9498	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0805
<65	289	9 (3.1)	280 (96.9)	NE (NE, NE)	126	1 (0.8)	125 (99.2)	NE (NE, NE)	2.0138 (0.2445, 16.5856) 0.5152	0.5072	
>=65	82	2 (2.4)	80 (97.6)	NE (NE, NE)	46	3 (6.5)	43 (93.5)	NE (NE, NE)	0.2517 (0.0409, 1.5471) 0.1365	0.1096	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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SOC: Investigations; PT: Electrocardiogram QT prolonged

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0059
<75	357	11 (3.1)	346 (96.9)	NE (NE, NE)	163	1 (0.6)	162 (99.4)	NE (NE, NE)	2.5506 (0.3188, 20.4060) 0.3775	0.3610	
>=75	14	0	14 (100)	NE (NE, NE)	9	3 (33.3)	6 (66.7)	NE (0.7, NE)	0.0000 (0.0000, ) 0.9973	0.0185	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.8506
White	175	6 (3.4)	169 (96.6)	NE (NE, NE)	85	2 (2.4)	83 (97.6)	NE (NE, NE)	0.8564 (0.1633, 4.4902) 0.8545	0.8548	
Non-White	196	5 (2.6)	191 (97.4)	NE (NE, NE)	86	2 (2.3)	84 (97.7)	NE (NE, NE)	0.5011 (0.0916, 2.7414) 0.4255	0.4175	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.7474
Asia	147	5 (3.4)	142 (96.6)	NE (NE, NE)	63	2 (3.2)	61 (96.8)	NE (NE, NE)	0.4889 (0.0899, 2.6585) 0.4075	0.3987	
North America	58	1 (1.7)	57 (98.3)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9986	0.8312	
Europe + Israel	166	5 (3.0)	161 (97.0)	NE (NE, NE)	81	2 (2.5)	79 (97.5)	NE (NE, NE)	0.8689 (0.1625, 4.6467) 0.8695	0.8698	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Electrocardiogram QT prolonged

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.8446
0	199	6 (3.0)	193 (97.0)	NE (NE, NE)	95	2 (2.1)	93 (97.9)	NE (NE, NE)	0.5886 (0.1131, 3.0625) 0.5288	0.5246	
1	172	5 (2.9)	167 (97.1)	NE (NE, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	0.8017 (0.1488, 4.3191) 0.7970	0.7971	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Electrocardiogram QT prolonged

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.2358
0	60	2 (3.3)	58 (96.7)	NE (NE, NE)	31	2 (6.5)	29 (93.5)	NE (NE, NE)	0.3167 (0.0381, 2.6300) 0.2871	0.2652	
1	107	3 (2.8)	104 (97.2)	NE (NE, NE)	48	1 (2.1)	47 (97.9)	NE (NE, NE)	1.1029 (0.1134, 10.7287) 0.9327	0.9327	
2	114	5 (4.4)	109 (95.6)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	NE (NE, NE) 0.9949	0.3668	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Electrocardiogram QT prolonged

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	1 (1.1)	89 (98.9)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (7.1, NE)	0.1067 (0.0066, 1.7149) 0.1143	0.0539	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Electrocardiogram QT prolonged

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.3542
PD	173	4 (2.3)	169 (97.7)	NE (NE, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	0.4965 (0.0838, 2.9405)	0.4324	
PR	48	2 (4.2)	46 (95.8)	NE (NE, NE)	21	1 (4.8)	20 (95.2)	NE (NE, NE)	0.4404 (0.0280, 4.0502)	0.3708	
SD	82	2 (2.4)	80 (97.6)	NE (NE, NE)	54	0	54 (100)	NE (NE, NE)	0.3365 (0.3909)	0.2890	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Electrocardiogram QT prolonged

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.4705
Yes	37	1 (2.7)	36 (97.3)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9983	0.7815	
No	334	10 (3.0)	324 (97.0)	NE (NE, NE)	159	4 (2.5)	155 (97.5)	NE (NE, NE)	0.6556 (0.1970, 2.1820) 0.4913	0.4890	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Electrocardiogram QT prolonged

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.9999
Yes	24	0	24 (100)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE)		
No	347	11 (3.2)	336 (96.8)	NE (NE, NE)	165	4 (2.4)	161 (97.6)	NE (NE, NE)	0.6756 (0.2056, 2.2197) 0.5182	0.5163	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Electrocardiogram QT prolonged

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0903
Normal Function	201	5 (2.5)	196 (97.5)	NE (NE, NE)	80	1 (1.3)	79 (98.8)	NE (NE, NE)	1.0570 (0.1141, 9.7895) 0.9611	0.9611	
Mild Impairment	123	6 (4.9)	117 (95.1)	NE (NE, NE)	65	1 (1.5)	64 (98.5)	NE (NE, NE)	1.4884 (0.1692, 13.0936) 0.7200	0.7170	
Moderate Impairment	41	0	41 (100)	NE (NE, NE)	23	2 (8.7)	21 (91.3)	NE (NE, NE)	0.0000 (0.0000, ) 0.9968	0.0358	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Investigations; PT: Electrocardiogram QT prolonged

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.0333
Normal Function	170	5 (2.9)	165 (97.1)	NE (NE, NE)	88	4 (4.5)	84 (95.5)	NE (NE, NE)	0.4062 (0.1035, 1.5942) 0.1966	0.1839	
Mild Impairment	194	6 (3.1)	188 (96.9)	NE (NE, NE)	82	0	82 (100)	NE (NE, NE)	NE (NE, NE) 0.9943	0.3208	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Electrocardiogram QT prolonged

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.7581
Yes	331	9 (2.7)	322 (97.3)	NE (NE, NE)	146	3 (2.1)	143 (97.9)	NE (NE, NE)	0.6991 (0.1826, 2.6774) 0.6014	0.6001	
No	40	2 (5.0)	38 (95.0)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	0.7808 (0.0581, 10.4873) 0.8519	0.8516	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Electrocardiogram QT prolonged

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.1915
Positive	329	9 (2.7)	320 (97.3)	NE (NE, NE)	152	2 (1.3)	150 (98.7)	NE (NE, NE)	0.9501 (0.1968, 4.5868)	0.9492	
Negative	42	2 (4.8)	40 (95.2)	NE (NE, NE)	20	2 (10.0)	18 (90.0)	NE (NE, NE)	0.3456 (0.0446, 2.6762)	0.2894	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Electrocardiogram QT prolonged

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.2742
Positive	331	8 (2.4)	323 (97.6)	NE (NE, NE)	155	2 (1.3)	153 (98.7)	NE (NE, NE)	0.8977 (0.1824, 4.4191)	0.8944	
Negative	40	3 (7.5)	37 (92.5)	NE (10.4, NE)	17	2 (11.8)	15 (88.2)	NE (NE, NE)	0.2587 (0.0294, 2.2750)	0.1936	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.5386
HER2 IHC 1+	214	137 (64.0)	77 (36.0)	2.8 (1.2, 5.0)	100	59 (59.0)	41 (41.0)	1.4 (0.6, 4.4)	0.9089 (0.6675, 1.2374) 0.5439	0.5338	
HER2 IHC 2+/ISH Negative	157	111 (70.7)	46 (29.3)	1.6 (0.9, 2.9)	72	43 (59.7)	29 (40.3)	1.4 (0.7, 7.7)	1.0452 (0.7322, 1.4920) 0.8076	0.8182	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.2912
1	220	146 (66.4)	74 (33.6)	2.6 (1.3, 3.8)	94	61 (64.9)	33 (35.1)	1.4 (0.6, 2.6)	0.8557 (0.6324, 1.1579) 0.3125	0.2932	
>=2	150	101 (67.3)	49 (32.7)	1.5 (0.8, 5.0)	78	41 (52.6)	37 (47.4)	3.3 (0.7, NE)	1.1129 (0.7709, 1.6066) 0.5680	0.5598	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.4744
Yes	233	154 (66.1)	79 (33.9)	1.4 (0.8, 3.6)	112	67 (59.8)	45 (40.2)	1.4 (0.7, 3.3)	0.9529 (0.7117, 1.2757) 0.7456	0.7227	
No	98	70 (71.4)	28 (28.6)	2.7 (1.4, 7.7)	43	24 (55.8)	19 (44.2)	2.6 (0.5, NE)	1.1142 (0.6991, 1.7757) 0.6494	0.6481	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3806
<65	289	188 (65.1)	101 (34.9)	2.6 (1.4, 4.3)	126	73 (57.9)	53 (42.1)	1.2 (0.6, 4.4)	0.9317 (0.7084, 1.2254) 0.6128	0.5931	
>=65	82	60 (73.2)	22 (26.8)	0.9 (0.7, 2.8)	46	29 (63.0)	17 (37.0)	2.0 (0.7, 4.6)	1.1427 (0.7323, 1.7831) 0.5567	0.5559	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2589
<75	357	237 (66.4)	120 (33.6)	2.2 (1.4, 3.8)	163	97 (59.5)	66 (40.5)	1.4 (0.7, 2.9)	0.9355 (0.7363, 1.1885) 0.5852	0.5689	
>=75	14	11 (78.6)	3 (21.4)	0.9 (0.1, 3.6)	9	5 (55.6)	4 (44.4)	4.6 (0.1, NE)	1.8751 (0.6445, 5.4550) 0.2486	0.2443	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.0780
White	175	114 (65.1)	61 (34.9)	2.7 (1.3, 4.2)	85	55 (64.7)	30 (35.3)	0.7 (0.5, 1.7)	0.7816 (0.5639, 1.0832) 0.1389	0.1343	
Non-White	196	134 (68.4)	62 (31.6)	1.5 (0.8, 3.8)	86	46 (53.5)	40 (46.5)	2.9 (0.8, NE)	1.1962 (0.8530, 1.6774) 0.2991	0.3060	

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.2806
Asia	147	96 (65.3)	51 (34.7)	2.9 (1.2, 8.2)	63	31 (49.2)	32 (50.8)	4.4 (0.8, NE)	1.1204 (0.7428, 1.6899) 0.5878	0.5877	
North America	58	43 (74.1)	15 (25.9)	1.3 (0.5, 3.9)	28	15 (53.6)	13 (46.4)	2.0 (0.4, NE)	1.1933 (0.6578, 2.1649) 0.5608	0.5618	
Europe + Israel	166	109 (65.7)	57 (34.3)	2.1 (0.9, 3.5)	81	56 (69.1)	25 (30.9)	0.7 (0.5, 1.7)	0.8158 (0.5896, 1.1288) 0.2192	0.2044	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.1259
0	199	135 (67.8)	64 (32.2)	2.1 (1.2, 3.1)	95	50 (52.6)	45 (47.4)	2.8 (0.8, NE)	1.1583 (0.8354, 1.6061) 0.3781	0.3847	
1	172	113 (65.7)	59 (34.3)	2.5 (0.8, 4.1)	77	52 (67.5)	25 (32.5)	0.7 (0.5, 2.0)	0.7781 (0.5569, 1.0872) 0.1415	0.1329	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1580
0	60	38 (63.3)	22 (36.7)	2.7 (0.6, 8.2)	31	21 (67.7)	10 (32.3)	0.5 (0.1, 3.9)	0.6492 (0.3731, 1.1295) 0.1263	0.1215	
1	107	63 (58.9)	44 (41.1)	7.7 (2.6, 9.3)	48	30 (62.5)	18 (37.5)	1.7 (0.5, 6.3)	0.7598 (0.4898, 1.1786) 0.2201	0.2154	
2	114	82 (71.9)	32 (28.1)	0.8 (0.6, 1.5)	50	28 (56.0)	22 (44.0)	1.7 (0.7, NE)	1.2946 (0.8412, 1.9922) 0.2404	0.2408	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	65 (72.2)	25 (27.8)	1.5 (0.8, 3.4)	43	23 (53.5)	20 (46.5)	4.4 (0.6, NE)	1.2043 (0.7444, 1.9481) 0.4488	0.4548	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.5186
PD	173	103 (59.5)	70 (40.5)	3.4 (1.5, 7.7)	77	45 (58.4)	32 (41.6)	1.4 (0.6, 4.6)	0.7881 (0.5520, 1.1251)	0.1850	
PR	48	34 (70.8)	14 (29.2)	1.4 (0.2, 11.0)	21	12 (57.1)	9 (42.9)	1.7 (0.4, NE)	1.1589 (0.5913, 2.2712)	0.6851	
SD	82	61 (74.4)	21 (25.6)	1.2 (0.5, 2.4)	54	36 (66.7)	18 (33.3)	0.7 (0.3, 3.9)	1.0197 (0.6737, 1.5434)	0.9307	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.9057
Yes	37	21 (56.8)	16 (43.2)	2.7 (0.3, NE)	13	6 (46.2)	7 (53.8)	NE (0.1, NE)	1.1042 (0.4438, 2.7470)	0.8275	
No	334	227 (68.0)	107 (32.0)	2.1 (1.3, 3.5)	159	96 (60.4)	63 (39.6)	1.4 (0.7, 2.9)	0.9586 (0.7530, 1.2203)	0.7172	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.9790
Yes	24	15 (62.5)	9 (37.5)	1.6 (0.1, NE)	7	4 (57.1)	3 (42.9)	0.5 (0.1, NE)	0.9923 (0.3259, 3.0214) 0.9892	0.9822	
No	347	233 (67.1)	114 (32.9)	2.1 (1.3, 3.5)	165	98 (59.4)	67 (40.6)	1.4 (0.7, 3.3)	0.9603 (0.7564, 1.2191) 0.7391	0.7275	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0397
Normal Function	201	127 (63.2)	74 (36.8)	2.8 (1.5, 4.8)	80	52 (65.0)	28 (35.0)	0.7 (0.5, 2.2)	0.7292 (0.5247, 1.0134) 0.0600	0.0561	
Mild Impairment	123	84 (68.3)	39 (31.7)	1.4 (0.7, 4.0)	65	36 (55.4)	29 (44.6)	1.7 (0.5, NE)	1.1077 (0.7460, 1.6448) 0.6120	0.6213	
Moderate Impairment	41	33 (80.5)	8 (19.5)	0.8 (0.3, 3.6)	23	12 (52.2)	11 (47.8)	3.9 (0.5, NE)	1.7085 (0.8813, 3.3121) 0.1128	0.1071	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.6897
Normal Function	170	117 (68.8)	53 (31.2)	1.4 (0.8, 3.5)	88	54 (61.4)	34 (38.6)	1.4 (0.5, 4.4)	1.0333 (0.7465, 1.4303) 0.8435	0.8647	
Mild Impairment	194	128 (66.0)	66 (34.0)	2.6 (1.2, 4.4)	82	47 (57.3)	35 (42.7)	1.4 (0.7, 6.3)	0.9134 (0.6504, 1.2827) 0.6009	0.6027	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.7013
Yes	331	223 (67.4)	108 (32.6)	2.1 (1.2, 3.5)	146	88 (60.3)	58 (39.7)	1.4 (0.7, 3.3)	0.9774 (0.7619, 1.2539) 0.8573	0.8441	
No	40	25 (62.5)	15 (37.5)	2.4 (0.8, 18.6)	26	14 (53.8)	12 (46.2)	1.3 (0.1, NE)	0.8973 (0.4599, 1.7507) 0.7506	0.7730	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.2195
Positive	329	220 (66.9)	109 (33.1)	2.5 (1.4, 3.9)	152	87 (57.2)	65 (42.8)	1.7 (0.7, 4.4)	1.0083 (0.7846, 1.2959)	0.9483	0.9629
Negative	42	28 (66.7)	14 (33.3)	0.9 (0.3, 4.0)	20	15 (75.0)	5 (25.0)	0.4 (0.1, 3.9)	0.6969 (0.3694, 1.3145)	0.2647	0.2629

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.4116
Positive	331	224 (67.7)	107 (32.3)	2.1 (1.3, 3.6)	155	91 (58.7)	64 (41.3)	1.4 (0.7, 2.9)	0.9912 (0.7748, 1.2680)	0.9288	
Negative	40	24 (60.0)	16 (40.0)	1.5 (0.5, NE)	17	11 (64.7)	6 (35.3)	0.5 (0.1, 4.6)	0.7604 (0.3693, 1.5655)	0.4666	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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DE.T.4.8.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	Nsub	T-DXd (N=371)			TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
		No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]		
HER2 status											0.6804
HER2 IHC 1+	214	57 (26.6)	157 (73.4)	NE (NE, NE)	100	28 (28.0)	72 (72.0)	NE (NE, NE)	0.8278 (0.5241, 1.3076) 0.4179	0.4113	
HER2 IHC 2+/ISH Negative	157	53 (33.8)	104 (66.2)	NE (NE, NE)	72	22 (30.6)	50 (69.4)	NE (7.7, NE)	0.9196 (0.5561, 1.5207) 0.7439	0.7388	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.5047
1	220	65 (29.5)	155 (70.5)	NE (NE, NE)	94	30 (31.9)	64 (68.1)	NE (NE, NE)	0.7944 (0.5134, 1.2292) 0.3014	0.2957	
>=2	150	45 (30.0)	105 (70.0)	NE (NE, NE)	78	20 (25.6)	58 (74.4)	NE (7.7, NE)	0.9940 (0.5827, 1.6956) 0.9825	0.9780	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.3220
Yes	233	75 (32.2)	158 (67.8)	NE (NE, NE)	112	31 (27.7)	81 (72.3)	NE (NE, NE)	1.0287 (0.6739, 1.5704) 0.8955	0.9061	
No	98	22 (22.4)	76 (77.6)	NE (NE, NE)	43	12 (27.9)	31 (72.1)	NE (7.7, NE)	0.6540 (0.3216, 1.3301) 0.2411	0.2374	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8921
<65	289	86 (29.8)	203 (70.2)	NE (NE, NE)	126	37 (29.4)	89 (70.6)	NE (7.7, NE)	0.8762 (0.5934, 1.2937) 0.5061	0.4921	
>=65	82	24 (29.3)	58 (70.7)	NE (NE, NE)	46	13 (28.3)	33 (71.7)	NE (4.6, NE)	0.8741 (0.4421, 1.7284) 0.6989	0.6984	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5213
<75	357	104 (29.1)	253 (70.9)	NE (NE, NE)	163	47 (28.8)	116 (71.2)	NE (NE, NE)	0.8593 (0.6064, 1.2178) 0.3940	0.3866	
>=75	14	6 (42.9)	8 (57.1)	6.2 (0.9, NE)	9	3 (33.3)	6 (66.7)	NE (0.1, NE)	1.4015 (0.3501, 5.6107) 0.6334	0.6407	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.8466
White	175	61 (34.9)	114 (65.1)	NE (12.7, NE)	85	29 (34.1)	56 (65.9)	NE (4.6, NE)	0.8567 (0.5478, 1.3398) 0.4978	0.4905	
Non-White	196	49 (25.0)	147 (75.0)	NE (NE, NE)	86	20 (23.3)	66 (76.7)	NE (NE, NE)	0.9439 (0.5579, 1.5970) 0.8297	0.8261	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.3767
Asia	147	33 (22.4)	114 (77.6)	NE (NE, NE)	63	12 (19.0)	51 (81.0)	NE (7.7, NE)	1.0145 (0.5193, 1.9821) 0.9664	0.9660	
North America	58	35 (60.3)	23 (39.7)	4.2 (0.7, 11.8)	28	13 (46.4)	15 (53.6)	2.0 (0.6, NE)	1.1133 (0.5815, 2.1315) 0.7460	0.7615	
Europe + Israel	166	42 (25.3)	124 (74.7)	NE (NE, NE)	81	25 (30.9)	56 (69.1)	NE (NE, NE)	0.7023 (0.4264, 1.1566) 0.1650	0.1594	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.6899
0	199	62 (31.2)	137 (68.8)	NE (NE, NE)	95	27 (28.4)	68 (71.6)	NE (NE, NE)	0.9568 (0.6066, 1.5093) 0.8496	0.8441	
1	172	48 (27.9)	124 (72.1)	NE (NE, NE)	77	23 (29.9)	54 (70.1)	NE (7.7, NE)	0.7789 (0.4702, 1.2905) 0.3321	0.3278	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1767
0	60	18 (30.0)	42 (70.0)	NE (NE, NE)	31	13 (41.9)	18 (58.1)	NE (0.5, NE)	0.5861 (0.2841, 1.2091) 0.1482	0.1422	
1	107	22 (20.6)	85 (79.4)	NE (NE, NE)	48	14 (29.2)	34 (70.8)	NE (NE, NE)	0.6180 (0.3149, 1.2127) 0.1617	0.1577	
2	114	42 (36.8)	72 (63.2)	NE (12.7, NE)	50	12 (24.0)	38 (76.0)	NE (NE, NE)	1.4129 (0.7397, 2.6987) 0.2952	0.2924	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	28 (31.1)	62 (68.9)	NE (NE, NE)	43	11 (25.6)	32 (74.4)	NE (7.7, NE)	1.0118 (0.4984, 2.0538) 0.9742	0.9756	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.0936
PD	173	44 (25.4)	129 (74.6)	NE (NE, NE)	77	22 (28.6)	55 (71.4)	NE (NE, NE)	0.7090 (0.4224, 1.1900)	0.1921	
PR	48	18 (37.5)	30 (62.5)	16.2 (12.7, NE)	21	3 (14.3)	18 (85.7)	NE (NE, NE)	2.4783 (0.7211, 8.5174)	0.1386	
SD	82	25 (30.5)	57 (69.5)	NE (NE, NE)	54	21 (38.9)	33 (61.1)	NE (2.3, NE)	0.6617 (0.3675, 1.1913)	0.1633	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.8909
Yes	37	8 (21.6)	29 (78.4)	NE (NE, NE)	13	3 (23.1)	10 (76.9)	NE (0.7, NE)	0.8835 (0.2331, 3.3480)	0.8545	
No	334	102 (30.5)	232 (69.5)	NE (NE, NE)	159	47 (29.6)	112 (70.4)	NE (NE, NE)	0.8554 (0.6183, 1.2442)	0.4552	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.4179
Yes	24	6 (25.0)	18 (75.0)	NE (NE, NE)	7	3 (42.9)	4 (57.1)	NE (0.1, NE)	0.5295 (0.1321, 2.1227) 0.3695	0.3644	
No	347	104 (30.0)	243 (70.0)	NE (NE, NE)	165	47 (28.5)	118 (71.5)	NE (NE, NE)	0.8931 (0.6302, 1.2657) 0.5251	0.5173	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	Nsub	T-DXd (N=371)			Nsub	TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
		No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.8980
Normal Function	201	63 (31.3)	138 (68.7)	NE (NE, NE)	80	26 (32.5)	54 (67.5)	NE (7.7, NE)	0.7954 (0.4993, 1.2669) 0.3351	0.3278	
Mild Impairment	123	32 (26.0)	91 (74.0)	NE (NE, NE)	65	17 (26.2)	48 (73.8)	NE (NE, NE)	0.8632 (0.4768, 1.5630) 0.6273	0.6217	
Moderate Impairment	41	14 (34.1)	27 (65.9)	NE (6.4, NE)	23	7 (30.4)	16 (69.6)	NE (2.3, NE)	1.0233 (0.4120, 2.5415) 0.9605	0.9617	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.6326
Normal Function	170	50 (29.4)	120 (70.6)	NE (NE, NE)	88	28 (31.8)	60 (68.2)	NE (7.7, NE)	0.7885 (0.4928, 1.2616) 0.3217	0.3110	
Mild Impairment	194	58 (29.9)	136 (70.1)	NE (NE, NE)	82	22 (26.8)	60 (73.2)	NE (NE, NE)	0.9444 (0.5759, 1.5487) 0.8208	0.8193	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1291
Yes	331	100 (30.2)	231 (69.8)	NE (NE, NE)	146	40 (27.4)	106 (72.6)	NE (NE, NE)	0.9665 (0.6677, 1.3990) 0.8566	0.8501	
No	40	10 (25.0)	30 (75.0)	NE (NE, NE)	26	10 (38.5)	16 (61.5)	NE (0.7, NE)	0.4662 (0.1889, 1.1503) 0.0977	0.0917	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.1749
Positive	329	94 (28.6)	235 (71.4)	NE (NE, NE)	152	39 (25.7)	113 (74.3)	NE (NE, NE)	0.9648 (0.6617, 1.4068)	0.8457	
Negative	42	16 (38.1)	26 (61.9)	NE (4.0, NE)	20	11 (55.0)	9 (45.0)	2.6 (0.2, NE)	0.5146 (0.2347, 1.1282)	0.0896	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.5957
Positive	331	96 (29.0)	235 (71.0)	NE (NE, NE)	155	43 (27.7)	112 (72.3)	NE (NE, NE)	0.8980 (0.6243, 1.2915)	0.5541	
Negative	40	14 (35.0)	26 (65.0)	NE (6.0, NE)	17	7 (41.2)	10 (58.8)	4.6 (0.3, NE)	0.5616 (0.2689, 1.7166)	0.4055	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Asthenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0021
HER2 IHC 1+	214	37 (17.3)	177 (82.7)	NE (NE, NE)	100	21 (21.0)	79 (79.0)	NE (NE, NE)	0.6751 (0.3914, 1.1646) 0.1579	0.1537	
HER2 IHC 2+/ISH Negative	157	33 (21.0)	124 (79.0)	NE (NE, NE)	72	4 (5.6)	68 (94.4)	NE (NE, NE)	3.7048 (1.3089, 10.4859) 0.0136	0.0082	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Asthenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.9859
1	220	42 (19.1)	178 (80.9)	NE (NE, NE)	94	14 (14.9)	80 (85.1)	NE (NE, NE)	1.1993 (0.6534, 2.2013) 0.5575	0.5628	
>=2	150	28 (18.7)	122 (81.3)	NE (NE, NE)	78	11 (14.1)	67 (85.9)	NE (NE, NE)	1.1059 (0.5425, 2.2544) 0.7818	0.7865	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: General disorders and administration site conditions; PT: Asthenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											
Yes	233	49 (21.0)	184 (79.0)	NE (NE, NE)	112	19 (17.0)	93 (83.0)	NE (NE, NE)	1.1349 (0.6651, 1.9367) 0.6425	0.6543	0.4238
No	98	18 (18.4)	80 (81.6)	NE (NE, NE)	43	4 (9.3)	39 (90.7)	NE (NE, NE)	1.8274 (0.6139, 5.4395) 0.2787	0.2724	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Asthenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8146
<65	289	54 (18.7)	235 (81.3)	NE (NE, NE)	126	17 (13.5)	109 (86.5)	NE (NE, NE)	1.2264 (0.7072, 2.1270) 0.4675	0.4726	
>=65	82	16 (19.5)	66 (80.5)	NE (NE, NE)	46	8 (17.4)	38 (82.6)	NE (NE, NE)	1.0619 (0.4512, 2.4989) 0.8907	0.8927	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: General disorders and administration site conditions; PT: Asthenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1641
<75	357	68 (19.0)	289 (81.0)	NE (NE, NE)	163	25 (15.3)	138 (84.7)	NE (NE, NE)	1.0960 (0.6894, 1.7423) 0.6984	0.7067	
>=75	14	2 (14.3)	12 (85.7)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9978	0.2382	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Asthenia

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.2687
White	175	38 (21.7)	137 (78.3)	NE (NE, NE)	85	17 (20.0)	68 (80.0)	NE (NE, NE)	0.9421 (0.5288, 1.6783) 0.8396	0.8329	
Non-White	196	32 (16.3)	164 (83.7)	NE (NE, NE)	86	8 (9.3)	78 (90.7)	NE (NE, NE)	1.6433 (0.7528, 3.5873) 0.2124	0.2099	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.0941
Asia	147	13 (8.8)	134 (91.2)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (NE, NE)	4.4172 (0.5693, 34.2700) 0.1553	0.1203	
North America	58	3 (5.2)	55 (94.8)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9968	0.3458	
Europe + Israel	166	54 (32.5)	112 (67.5)	NE (NE, NE)	81	24 (29.6)	57 (70.4)	NE (NE, NE)	1.0654 (0.6572, 1.7271) 0.7973	0.8181	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.7438
0	199	28 (14.1)	171 (85.9)	NE (NE, NE)	95	9 (9.5)	86 (90.5)	NE (NE, NE)	1.3757 (0.6482, 2.9198) 0.4061	0.4065	
1	172	42 (24.4)	130 (75.6)	NE (18.3, NE)	77	16 (20.8)	61 (79.2)	NE (NE, NE)	1.0135 (0.5634, 1.8231) 0.9643	0.9739	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.3634
0	60	7 (11.7)	53 (88.3)	NE (NE, NE)	31	3 (9.7)	28 (90.3)	NE (NE, NE)	1.1365 (0.2930, 4.4080) 0.8532	0.8549	
1	107	20 (18.7)	87 (81.3)	NE (NE, NE)	48	8 (16.7)	40 (83.3)	NE (NE, NE)	1.1486 (0.5054, 2.6105) 0.7409	0.7485	
2	114	24 (21.1)	90 (78.9)	NE (NE, NE)	50	11 (22.0)	39 (78.0)	NE (NE, NE)	0.7791 (0.3762, 1.6132) 0.5014	0.4973	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	19 (21.1)	71 (78.9)	NE (18.9, NE)	43	3 (7.0)	40 (93.0)	NE (NE, NE)	2.5758 (0.7541, 8.7988) 0.1311	0.1171	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.6330
PD	173	32 (18.5)	141 (81.5)	NE (NE, NE)	77	12 (15.6)	65 (84.4)	NE (NE, NE)	1.0909 (0.5599, 2.1257) 0.7982	0.8053	
PR	48	12 (25.0)	36 (75.0)	18.9 (14.2, NE)	21	5 (23.8)	16 (76.2)	NE (2.5, NE)	0.6852 (0.2271, 2.0674) 0.5023	0.4951	
SD	82	14 (17.1)	68 (82.9)	NE (NE, NE)	54	5 (9.3)	49 (90.7)	NE (NE, NE)	1.7873 (0.6411, 4.9833) 0.2670	0.2635	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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Reported history of CNS metastases											0.9579
Yes	37	4 (10.8)	33 (89.2)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	1.3683 (0.1529, 12.2441)	0.7781	
No	334	66 (19.8)	268 (80.2)	NE (NE, NE)	159	24 (15.1)	135 (84.9)	NE (NE, NE)	1.1657 (0.7270, 1.8691)	0.5321	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.3424
Yes	24	2 (8.3)	22 (91.7)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9973	0.4401	
No	347	68 (19.6)	279 (80.4)	NE (NE, NE)	165	25 (15.2)	140 (84.8)	NE (NE, NE)	1.1472 (0.7219, 1.8233) 0.5612	0.5693	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Asthenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.1700
Normal Function	201	34 (16.9)	167 (83.1)	NE (NE, NE)	80	15 (18.8)	65 (81.3)	NE (NE, NE)	0.7763 (0.4202, 1.4342) 0.4189	0.4116	
Mild Impairment	123	24 (19.5)	99 (80.5)	NE (18.9, NE)	65	8 (12.3)	57 (87.7)	NE (NE, NE)	1.4330 (0.6374, 3.2216) 0.3841	0.3849	
Moderate Impairment	41	10 (24.4)	31 (75.6)	NE (18.3, NE)	23	2 (8.7)	21 (91.3)	NE (NE, NE)	2.6674 (0.5756, 12.3611) 0.2098	0.1934	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: General disorders and administration site conditions; PT: Asthenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.2410
Normal Function	170	35 (20.6)	135 (79.4)	NE (18.9, NE)	88	11 (12.5)	77 (87.5)	NE (NE, NE)	1.5369 (0.7756, 3.0455) 0.2180	0.2173	
Mild Impairment	194	34 (17.5)	160 (82.5)	NE (NE, NE)	82	14 (17.1)	68 (82.9)	NE (NE, NE)	0.8755 (0.4668, 1.6421) 0.6786	0.6737	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: General disorders and administration site conditions; PT: Asthenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1656
Yes	331	63 (19.0)	268 (81.0)	NE (NE, NE)	146	24 (16.4)	122 (83.6)	NE (NE, NE)	1.0396 (0.6472, 1.6700) 0.8723	0.8801	
No	40	7 (17.5)	33 (82.5)	NE (18.3, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	3.9390 (0.4740, 32.7346) 0.2045	0.1709	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.9409
Positive	329	65 (19.8)	264 (80.2)	NE (NE, NE)	152	23 (15.1)	129 (84.9)	NE (NE, NE)	1.1813 (0.7315, 1.9077)	0.4957	0.5029
Negative	42	5 (11.9)	37 (88.1)	NE (18.3, NE)	20	2 (10.0)	18 (90.0)	NE (3.9, NE)	0.8894 (0.1620, 4.8844)	0.8927	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: General disorders and administration site conditions; PT: Asthenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.2486
Positive	331	68 (20.5)	263 (79.5)	NE (NE, NE)	155	23 (14.8)	132 (85.2)	NE (NE, NE)	1.2498 (0.7756, 2.0139)	0.3650	
Negative	40	2 (5.0)	38 (95.0)	NE (NE, NE)	17	2 (11.8)	15 (88.2)	NE (3.9, NE)	0.3338 (0.0461, 2.4152)	0.2545	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.2254
HER2 IHC 1+	214	23 (10.7)	191 (89.3)	NE (NE, NE)	100	14 (14.0)	86 (86.0)	NE (NE, NE)	0.4610 (0.2288, 0.9287) 0.0302	0.0269	
HER2 IHC 2+/ISH Negative	157	23 (14.6)	134 (85.4)	NE (NE, NE)	72	8 (11.1)	64 (88.9)	NE (11.0, NE)	0.7967 (0.3493, 1.8168) 0.5889	0.5873	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.1074
1	220	26 (11.8)	194 (88.2)	NE (NE, NE)	94	16 (17.0)	78 (83.0)	NE (11.0, NE)	0.4332 (0.2275, 0.8249) 0.0109	0.0091	
>=2	150	20 (13.3)	130 (86.7)	NE (NE, NE)	78	6 (7.7)	72 (92.3)	NE (NE, NE)	0.9964 (0.3873, 2.5631) 0.9940	0.9940	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.6553
Yes	233	25 (10.7)	208 (89.3)	NE (NE, NE)	112	15 (13.4)	97 (86.6)	NE (11.0, NE)	0.4521 (0.2314, 0.8834) 0.0202	0.0176	
No	98	14 (14.3)	84 (85.7)	NE (NE, NE)	43	6 (14.0)	37 (86.0)	NE (NE, NE)	0.6846 (0.2559, 1.8318) 0.4505	0.4480	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9603
<65	289	38 (13.1)	251 (86.9)	NE (NE, NE)	126	17 (13.5)	109 (86.5)	NE (11.0, NE)	0.5757 (0.3180, 1.0424) 0.0683	0.0656	
>=65	82	8 (9.8)	74 (90.2)	NE (NE, NE)	46	5 (10.9)	41 (89.1)	NE (NE, NE)	0.5856 (0.1851, 1.8522) 0.3623	0.3589	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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SOC: General disorders and administration site conditions; PT: Pyrexia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6331
<75	357	44 (12.3)	313 (87.7)	NE (NE, NE)	163	21 (12.9)	142 (87.1)	NE (NE, NE)	0.5659 (0.3294, 0.9721) 0.0392	0.0370	
>=75	14	2 (14.3)	12 (85.7)	NE (7.5, NE)	9	1 (11.1)	8 (88.9)	NE (0.1, NE)	0.9118 (0.0794, 10.4685) 0.9409	0.9408	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Pyrexia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.9268
White	175	22 (12.6)	153 (87.4)	NE (NE, NE)	85	11 (12.9)	74 (87.1)	NE (11.0, NE)	0.5391 (0.2540, 1.1444) 0.1077	0.1032	
Non-White	196	24 (12.2)	172 (87.8)	NE (NE, NE)	86	11 (12.8)	75 (87.2)	NE (NE, NE)	0.6275 (0.2997, 1.3140) 0.2165	0.2143	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.9077
Asia	147	18 (12.2)	129 (87.8)	NE (NE, NE)	63	8 (12.7)	55 (87.3)	NE (NE, NE)	0.6104 (0.2567, 1.4512) 0.2639	0.2623	
North America	58	5 (8.6)	53 (91.4)	NE (NE, NE)	28	3 (10.7)	25 (89.3)	NE (NE, NE)	0.6740 (0.1605, 2.8297) 0.5899	0.5876	
Europe + Israel	166	23 (13.9)	143 (86.1)	NE (NE, NE)	81	11 (13.6)	70 (86.4)	NE (11.0, NE)	0.5654 (0.2687, 1.1896) 0.1330	0.1286	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: General disorders and administration site conditions; PT: Pyrexia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.0798
0	199	30 (15.1)	169 (84.9)	NE (NE, NE)	95	10 (10.5)	85 (89.5)	NE (NE, NE)	0.8591 (0.4118, 1.7924) 0.6857	0.6863	
1	172	16 (9.3)	156 (90.7)	NE (NE, NE)	77	12 (15.6)	65 (84.4)	NE (NE, NE)	0.3761 (0.1715, 0.8246) 0.0146	0.0114	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.3119
0	60	12 (20.0)	48 (80.0)	18.6 (18.6, NE)	31	4 (12.9)	27 (87.1)	NE (NE, NE)	0.9308 (0.2853, 3.0368) 0.9053	0.9061	
1	107	8 (7.5)	99 (92.5)	NE (NE, NE)	48	9 (18.8)	39 (81.3)	NE (11.0, NE)	0.2606 (0.0981, 0.6926) 0.0070	0.0040	
2	114	19 (16.7)	95 (83.3)	NE (NE, NE)	50	6 (12.0)	44 (88.0)	NE (NE, NE)	0.8430 (0.3273, 2.1713) 0.7236	0.7245	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: General disorders and administration site conditions; PT: Pyrexia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	7 (7.8)	83 (92.2)	NE (NE, NE)	43	3 (7.0)	40 (93.0)	NE (NE, NE)	0.6057 (0.1465, 2.5043) 0.4887	0.4874	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.4164
PD	173	23 (13.3)	150 (86.7)	NE (18.6, NE)	77	9 (11.7)	68 (88.3)	NE (NE, NE)	0.6114 (0.2716, 1.3764)	0.2320	
PR	48	3 (6.3)	45 (93.8)	NE (NE, NE)	21	3 (14.3)	18 (85.7)	NE (NE, NE)	0.3264 (0.0645, 1.6534)	0.1557	
SD	82	15 (18.3)	67 (81.7)	NE (NE, NE)	54	8 (14.8)	46 (85.2)	NE (11.0, NE)	0.8969 (0.3741, 2.1506)	0.8087	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.3940
Yes	37	6 (16.2)	31 (83.8)	NE (18.1, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	1.0786 (0.1224, 9.5027)	0.9456	
No	334	40 (12.0)	294 (88.0)	NE (NE, NE)	159	21 (13.2)	138 (86.8)	NE (NE, NE)	0.5495 (0.3172, 0.9517)	0.0306	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0385
Yes	24	6 (25.0)	18 (75.0)	18.1 (10.3, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9960	0.2642	
No	347	40 (11.5)	307 (88.5)	NE (NE, NE)	165	22 (13.3)	143 (86.7)	NE (NE, NE)	0.5210 (0.3032, 0.8954) 0.0183	0.0167	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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 [c] Two-sided p-value from unstratified log-rank test.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0948
Normal Function	201	28 (13.9)	173 (86.1)	NE (NE, NE)	80	12 (15.0)	68 (85.0)	NE (NE, NE)	0.5508 (0.2725, 1.1133) 0.0967	0.0924	
Mild Impairment	123	11 (8.9)	112 (91.1)	NE (18.6, NE)	65	9 (13.8)	56 (86.2)	NE (11.0, NE)	0.3105 (0.1182, 0.8156) 0.0176	0.0128	
Moderate Impairment	41	7 (17.1)	34 (82.9)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	3.2644 (0.3992, 26.6946) 0.2698	0.2412	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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[c] Two-sided p-value from unstratified log-rank test.

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SOC: General disorders and administration site conditions; PT: Pyrexia

Subgroup	Nsub	T-DXd (N=371)			Nsub	TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
		No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.8236
Normal Function	170	22 (12.9)	148 (87.1)	NE (NE, NE)	88	11 (12.5)	77 (87.5)	NE (NE, NE)	0.6933 (0.3300, 1.4569) 0.3337	0.3324	
Mild Impairment	194	24 (12.4)	170 (87.6)	NE (18.6, NE)	82	11 (13.4)	71 (86.6)	NE (11.0, NE)	0.4688 (0.2193, 1.0020) 0.0506	0.0461	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Pyrexia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.4720
Yes	331	41 (12.4)	290 (87.6)	NE (NE, NE)	146	18 (12.3)	128 (87.7)	NE (NE, NE)	0.6376 (0.3609, 1.1264) 0.1212	0.1194	
No	40	5 (12.5)	35 (87.5)	NE (18.6, NE)	26	4 (15.4)	22 (84.6)	NE (NE, NE)	0.3406 (0.0726, 1.5987) 0.1722	0.1555	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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[c] Two-sided p-value from unstratified log-rank test.

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SOC: General disorders and administration site conditions; PT: Pyrexia

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.3129
Positive	329	38 (11.6)	291 (88.4)	NE (NE, NE)	152	20 (13.2)	132 (86.8)	NE (NE, NE)	0.5251 (0.2991, 0.9218)	0.0229	
Negative	42	8 (19.0)	34 (81.0)	NE (7.5, NE)	20	2 (10.0)	18 (90.0)	NE (NE, NE)	1.1120 (0.2189, 5.6478)	0.8981	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: General disorders and administration site conditions; PT: Pyrexia

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.1909
Positive	331	39 (11.8)	292 (88.2)	NE (NE, NE)	155	21 (13.5)	134 (86.5)	NE (NE, NE)	0.5240 (0.3019, 0.9095)	0.0198	
Negative	40	7 (17.5)	33 (82.5)	NE (NE, NE)	17	1 (5.9)	16 (94.1)	NE (NE, NE)	1.5219 (0.1726, 13.4201)	0.7033	

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.4461
HER2 IHC 1+	214	22 (10.3)	192 (89.7)	NE (NE, NE)	100	6 (6.0)	94 (94.0)	NE (NE, NE)	1.4630 (0.5886, 3.6361) 0.4127	0.4111	
HER2 IHC 2+/ISH Negative	157	11 (7.0)	146 (93.0)	NE (NE, NE)	72	5 (6.9)	67 (93.1)	NE (NE, NE)	0.9359 (0.3245, 2.6994) 0.9024	0.9077	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.2464
1	220	16 (7.3)	204 (92.7)	NE (NE, NE)	94	7 (7.4)	87 (92.6)	NE (NE, NE)	0.9164 (0.3764, 2.2314) 0.8476	0.8457	
>=2	150	17 (11.3)	133 (88.7)	NE (NE, NE)	78	4 (5.1)	74 (94.9)	NE (NE, NE)	1.7851 (0.5945, 5.3607) 0.3016	0.2946	

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.4242
Yes	233	17 (7.3)	216 (92.7)	NE (NE, NE)	112	5 (4.5)	107 (95.5)	NE (NE, NE)	1.4015 (0.5133, 3.8272) 0.5101	0.5078	
No	98	10 (10.2)	88 (89.8)	NE (NE, NE)	43	5 (11.6)	38 (88.4)	NE (NE, NE)	0.8244 (0.2811, 2.4178) 0.7251	0.7216	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5634
<65	289	21 (7.3)	268 (92.7)	NE (NE, NE)	126	5 (4.0)	121 (96.0)	NE (NE, NE)	1.5349 (0.5742, 4.1029) 0.3931	0.3874	
>=65	82	12 (14.6)	70 (85.4)	NE (NE, NE)	46	6 (13.0)	40 (87.0)	NE (NE, NE)	1.0829 (0.4059, 2.8891) 0.8737	0.8744	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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Age											0.2036
<75	357	32 (9.0)	325 (91.0)	NE (NE, NE)	163	9 (5.5)	154 (94.5)	NE (NE, NE)	1.4146 (0.6721, 2.9771) 0.3610	0.3576	
>=75	14	1 (7.1)	13 (92.9)	NE (NE, NE)	9	2 (22.2)	7 (77.8)	NE (0.4, NE)	0.3187 (0.0289, 3.5196) 0.3508	0.3248	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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Race											0.2659
White	175	2 (1.1)	173 (98.9)	NE (NE, NE)	85	0	85 (100)	NE (NE, NE)	NE (NE, NE) 0.9974	0.4822	
Non-White	196	31 (15.8)	165 (84.2)	NE (NE, NE)	86	11 (12.8)	75 (87.2)	NE (NE, NE)	1.1283 (0.5652, 2.2524) 0.7322	0.7333	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.3780
Asia	147	30 (20.4)	117 (79.6)	NE (NE, NE)	63	11 (17.5)	52 (82.5)	NE (NE, NE)	1.0749 (0.5370, 2.1516) 0.8383	0.8407	
North America	58	2 (3.4)	56 (96.6)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9977	0.5436	
Europe + Israel	166	1 (0.6)	165 (99.4)	NE (NE, NE)	81	0	81 (100)	NE (NE, NE)	NE (NE, NE) 0.9981	0.6025	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Malaise

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.0558
0	199	25 (12.6)	174 (87.4)	NE (NE, NE)	95	5 (5.3)	90 (94.7)	NE (NE, NE)	2.0592 (0.7843, 5.4060) 0.1425	0.1333	
1	172	8 (4.7)	164 (95.3)	NE (NE, NE)	77	6 (7.8)	71 (92.2)	NE (NE, NE)	0.5553 (0.1920, 1.6056) 0.2775	0.2705	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.8384
0	60	6 (10.0)	54 (90.0)	NE (NE, NE)	31	3 (9.7)	28 (90.3)	NE (NE, NE)	0.8428 (0.2064, 3.4413) 0.8117	0.8097	
1	107	6 (5.6)	101 (94.4)	NE (NE, NE)	48	2 (4.2)	46 (95.8)	NE (NE, NE)	1.3041 (0.2629, 6.4697) 0.7453	0.7446	
2	114	7 (6.1)	107 (93.9)	NE (NE, NE)	50	1 (2.0)	49 (98.0)	NE (NE, NE)	2.6285 (0.3214, 21.4989) 0.3674	0.3477	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: General disorders and administration site conditions; PT: Malaise

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	14 (15.6)	76 (84.4)	NE (NE, NE)	43	5 (11.6)	38 (88.4)	NE (NE, NE)	1.1192 (0.3993, 3.1364) 0.8305	0.8295	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Malaise

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.0864
PD	173	13 (7.5)	160 (92.5)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	4.8705 (0.6337, 37.4335)	0.0924	
PR	48	4 (8.3)	44 (91.7)	NE (NE, NE)	21	3 (14.3)	18 (85.7)	NE (NE, NE)	0.5250 (0.1172, 2.3514)	0.3918	
SD	82	10 (12.2)	72 (87.8)	NE (NE, NE)	54	7 (13.0)	47 (87.0)	NE (NE, NE)	0.8877 (0.3373, 2.3363)	0.7996	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: General disorders and administration site conditions; PT: Malaise

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.1666
Yes	37	4 (10.8)	33 (89.2)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9959	0.2357	
No	334	29 (8.7)	305 (91.3)	NE (NE, NE)	159	11 (6.9)	148 (93.1)	NE (NE, NE)	1.0876 (0.5405, 2.1887) 0.8139	0.8142	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: General disorders and administration site conditions; PT: Malaise

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.1669
Yes	24	4 (16.7)	20 (83.3)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9961	0.2626	
No	347	29 (8.4)	318 (91.6)	NE (NE, NE)	165	11 (6.7)	154 (93.3)	NE (NE, NE)	1.0702 (0.5316, 2.1544) 0.8493	0.8493	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.4356
Normal Function	201	15 (7.5)	186 (92.5)	NE (NE, NE)	80	2 (2.5)	78 (97.5)	NE (NE, NE)	2.5071 (0.5690, 11.0469) 0.2245	0.2090	
Mild Impairment	123	12 (9.8)	111 (90.2)	NE (NE, NE)	65	6 (9.2)	59 (90.8)	NE (NE, NE)	0.8916 (0.3308, 2.4029) 0.8205	0.8189	
Moderate Impairment	41	4 (9.8)	37 (90.2)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	2.2756 (0.2542, 20.3697) 0.4622	0.4496	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.5428
Normal Function	170	14 (8.2)	156 (91.8)	NE (NE, NE)	88	6 (6.8)	82 (93.2)	NE (NE, NE)	1.1103 (0.4249, 2.9012) 0.8309	0.8305	
Mild Impairment	194	18 (9.3)	176 (90.7)	NE (NE, NE)	82	4 (4.9)	78 (95.1)	NE (NE, NE)	1.5678 (0.5261, 4.6725) 0.4196	0.4163	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.5602
Yes	331	29 (8.8)	302 (91.2)	NE (NE, NE)	146	10 (6.8)	136 (93.2)	NE (NE, NE)	1.1256 (0.5463, 2.3194) 0.7484	0.7480	
No	40	4 (10.0)	36 (90.0)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	2.2931 (0.2520, 20.8674) 0.4614	0.4507	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: General disorders and administration site conditions; PT: Malaise

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.4040
Positive	329	27 (8.2)	302 (91.8)	NE (NE, NE)	152	10 (6.6)	142 (93.4)	NE (NE, NE)	1.1069 (0.5337, 2.2957)	0.7860	
Negative	42	6 (14.3)	36 (85.7)	NE (NE, NE)	20	1 (5.0)	19 (95.0)	NE (NE, NE)	2.1085 (0.2432, 18.2828)	0.4846	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Malaise

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.5072
Positive	331	27 (8.2)	304 (91.8)	NE (NE, NE)	155	10 (6.5)	145 (93.5)	NE (NE, NE)	1.1263 (0.5431, 2.3358)	0.7492	
Negative	40	6 (15.0)	34 (85.0)	NE (NE, NE)	17	1 (5.9)	16 (94.1)	NE (NE, NE)	1.8409 (0.2115, 16.0255)	0.5804	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: General disorders and administration site conditions; PT: Oedema peripheral

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.1927
HER2 IHC 1+	214	16 (7.5)	198 (92.5)	NE (NE, NE)	100	4 (4.0)	96 (96.0)	NE (NE, NE)	1.1173 (0.3619, 3.4495) 0.8471	0.8461	
HER2 IHC 2+/ISH Negative	157	9 (5.7)	148 (94.3)	NE (NE, NE)	72	6 (8.3)	66 (91.7)	NE (NE, NE)	0.4195 (0.1446, 1.2175) 0.1101	0.1004	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: General disorders and administration site conditions; PT: Oedema peripheral

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.9117
1	220	16 (7.3)	204 (92.7)	NE (NE, NE)	94	6 (6.4)	88 (93.6)	NE (NE, NE)	0.6933 (0.2644, 1.8181) 0.4565	0.4542	
>=2	150	9 (6.0)	141 (94.0)	NE (NE, NE)	78	4 (5.1)	74 (94.9)	NE (NE, NE)	0.7483 (0.2208, 2.5357) 0.6415	0.6405	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: General disorders and administration site conditions; PT: Oedema peripheral

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.2862
Yes	233	14 (6.0)	219 (94.0)	NE (NE, NE)	112	8 (7.1)	104 (92.9)	NE (NE, NE)	0.4301 (0.1726, 1.0717) 0.0701	0.0632	
No	98	8 (8.2)	90 (91.8)	NE (NE, NE)	43	2 (4.7)	41 (95.3)	NE (NE, NE)	1.3623 (0.2850, 6.5122) 0.6985	0.6963	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: General disorders and administration site conditions; PT: Oedema peripheral

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8459
<65	289	14 (4.8)	275 (95.2)	NE (NE, NE)	126	5 (4.0)	121 (96.0)	NE (NE, NE)	0.7357 (0.2575, 2.1021) 0.5666	0.5658	
>=65	82	11 (13.4)	71 (86.6)	NE (NE, NE)	46	5 (10.9)	41 (89.1)	NE (NE, NE)	0.8098 (0.2740, 2.3931) 0.7028	0.7026	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: General disorders and administration site conditions; PT: Oedema peripheral

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6634
<75	357	23 (6.4)	334 (93.6)	NE (NE, NE)	163	9 (5.5)	154 (94.5)	NE (NE, NE)	0.7050 (0.3179, 1.5637) 0.3898	0.3880	
>=75	14	2 (14.3)	12 (85.7)	NE (5.9, NE)	9	1 (11.1)	8 (88.9)	NE (1.4, NE)	1.1579 (0.1045, 12.8332) 0.9049	0.9048	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.6840
White	175	13 (7.4)	162 (92.6)	NE (NE, NE)	85	6 (7.1)	79 (92.9)	NE (NE, NE)	0.6262 (0.2295, 1.7089) 0.3608	0.3568	
Non-White	196	12 (6.1)	184 (93.9)	NE (NE, NE)	86	4 (4.7)	82 (95.3)	NE (NE, NE)	0.8135 (0.2549, 2.5968) 0.7275	0.7278	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: General disorders and administration site conditions; PT: Oedema peripheral

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.6546
Asia	147	7 (4.8)	140 (95.2)	NE (NE, NE)	63	3 (4.8)	60 (95.2)	NE (NE, NE)	0.5147 (0.1273, 2.0802) 0.3513	0.3442	
North America	58	5 (8.6)	53 (91.4)	NE (NE, NE)	28	3 (10.7)	25 (89.3)	NE (5.1, NE)	0.4565 (0.1019, 2.0452) 0.3054	0.2947	
Europe + Israel	166	13 (7.8)	153 (92.2)	NE (NE, NE)	81	4 (4.9)	77 (95.1)	NE (NE, NE)	1.0772 (0.3423, 3.3892) 0.8989	0.8991	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Oedema peripheral

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.8546
0	199	12 (6.0)	187 (94.0)	NE (NE, NE)	95	5 (5.3)	90 (94.7)	NE (NE, NE)	0.5462 (0.1851, 1.6122) 0.2735	0.2672	
1	172	13 (7.6)	159 (92.4)	NE (NE, NE)	77	5 (6.5)	72 (93.5)	NE (NE, NE)	0.9258 (0.3254, 2.6343) 0.8852	0.8846	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.5206
0	60	2 (3.3)	58 (96.7)	NE (NE, NE)	31	2 (6.5)	29 (93.5)	NE (NE, NE)	0.4856 (0.0684, 3.4506) 0.4703	0.4607	
1	107	6 (5.6)	101 (94.4)	NE (NE, NE)	48	3 (6.3)	45 (93.8)	NE (NE, NE)	0.7867 (0.1954, 3.1678) 0.7357	0.7357	
2	114	9 (7.9)	105 (92.1)	NE (NE, NE)	50	4 (8.0)	46 (92.0)	NE (NE, NE)	0.4794 (0.1381, 1.6642) 0.2470	0.2379	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Oedema peripheral

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	8 (8.9)	82 (91.1)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	1.3048 (0.1571, 10.8380) 0.8054	0.8017	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Oedema peripheral

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.0536
PD	173	16 (9.2)	157 (90.8)	NE (NE, NE)	77	5 (6.5)	72 (93.5)	NE (NE, NE)	0.8897 (0.3162, 2.5031)	0.8240	
PR	48	0	48 (100)	NE (NE, NE)	21	2 (9.5)	19 (90.5)	NE (4.4, NE)	0.8247 (0.0000, )	0.0075	
SD	82	5 (6.1)	77 (93.9)	NE (NE, NE)	54	3 (5.6)	51 (94.4)	NE (NE, NE)	0.9977 (0.1600, 3.0254)	0.6269	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Oedema peripheral

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.3902
Yes	37	1 (2.7)	36 (97.3)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (2.1, NE)	0.3263 (0.0204, 5.2266)	0.4047	
No	334	24 (7.2)	310 (92.8)	NE (NE, NE)	159	9 (5.7)	150 (94.3)	NE (NE, NE)	0.4287 (0.3439, 1.6689)	0.4899	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Oedema peripheral

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.9998
Yes	24	0	24 (100)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE)		
No	347	25 (7.2)	322 (92.8)	NE (NE, NE)	165	10 (6.1)	155 (93.9)	NE (NE, NE)	0.7138 (0.3349, 1.5214) 0.3826	0.3809	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Oedema peripheral

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.3907
Normal Function	201	8 (4.0)	193 (96.0)	NE (NE, NE)	80	4 (5.0)	76 (95.0)	NE (NE, NE)	0.4783 (0.1380, 1.6577) 0.2449	0.2352	
Mild Impairment	123	12 (9.8)	111 (90.2)	NE (NE, NE)	65	5 (7.7)	60 (92.3)	NE (NE, NE)	0.7312 (0.2473, 2.1617) 0.5714	0.5701	
Moderate Impairment	41	5 (12.2)	36 (87.8)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	2.2488 (0.2612, 19.3628) 0.4607	0.4486	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Oedema peripheral

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.8482
Normal Function	170	9 (5.3)	161 (94.7)	NE (NE, NE)	88	4 (4.5)	84 (95.5)	NE (NE, NE)	0.5525 (0.1640, 1.8611) 0.3383	0.3322	
Mild Impairment	194	15 (7.7)	179 (92.3)	NE (NE, NE)	82	6 (7.3)	76 (92.7)	NE (NE, NE)	0.7074 (0.2680, 1.8670) 0.4845	0.4829	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Oedema peripheral

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.5690
Yes	331	21 (6.3)	310 (93.7)	NE (NE, NE)	146	9 (6.2)	137 (93.8)	NE (NE, NE)	0.6573 (0.2953, 1.4630) 0.3040	0.3012	
No	40	4 (10.0)	36 (90.0)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	1.2137 (0.1184, 12.4401) 0.8704	0.8703	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Oedema peripheral

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.1410
Positive	329	22 (6.7)	307 (93.3)	NE (NE, NE)	152	10 (6.6)	142 (93.4)	NE (NE, NE)	0.6154 (0.2853, 1.3274)	0.2123	
Negative	42	3 (7.1)	39 (92.9)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	0.2158 (NE, NE) 0.9968	0.3203	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Oedema peripheral

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.1684
Positive	331	22 (6.6)	309 (93.4)	NE (NE, NE)	155	10 (6.5)	145 (93.5)	NE (NE, NE)	0.6241 (0.2892, 1.3469)	0.2263	
Negative	40	3 (7.5)	37 (92.5)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	0.2297 (NE, NE) 0.9969	0.3473	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Chills

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.6645
HER2 IHC 1+	214	6 (2.8)	208 (97.2)	NE (NE, NE)	100	1 (1.0)	99 (99.0)	NE (NE, NE)	2.2331 (0.2650, 18.8160) 0.4600	0.4477	
HER2 IHC 2+/ISH Negative	157	7 (4.5)	150 (95.5)	NE (NE, NE)	72	2 (2.8)	70 (97.2)	NE (NE, NE)	1.1874 (0.2406, 5.8612) 0.8330	0.8335	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Chills

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.0511
1	220	7 (3.2)	213 (96.8)	NE (NE, NE)	94	0	94 (100)	NE (NE, NE)	NE (NE, NE) 0.9945	0.1107	
>=2	150	6 (4.0)	144 (96.0)	NE (NE, NE)	78	3 (3.8)	75 (96.2)	NE (NE, NE)	0.6572 (0.1515, 2.8507) 0.5750	0.5713	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: General disorders and administration site conditions; PT: Chills

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.1222
Yes	233	8 (3.4)	225 (96.6)	NE (NE, NE)	112	3 (2.7)	109 (97.3)	NE (NE, NE)	1.0498 (0.2750, 4.0077) 0.9433	0.9432	
No	98	5 (5.1)	93 (94.9)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9959	0.2282	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: General disorders and administration site conditions; PT: Chills

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6677
<65	289	11 (3.8)	278 (96.2)	NE (NE, NE)	126	2 (1.6)	124 (98.4)	NE (NE, NE)	1.6582 (0.3602, 7.6343) 0.5162	0.5119	
>=65	82	2 (2.4)	80 (97.6)	NE (NE, NE)	46	1 (2.2)	45 (97.8)	NE (NE, NE)	1.1153 (0.1011, 12.3012) 0.9290	0.9289	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Chills

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9999
<75	357	13 (3.6)	344 (96.4)	NE (NE, NE)	163	3 (1.8)	160 (98.2)	NE (NE, NE)	1.4938 (0.4189, 5.3264) 0.5361	0.5331	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Chills

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.1732
White	175	9 (5.1)	166 (94.9)	NE (NE, NE)	85	3 (3.5)	82 (96.5)	NE (NE, NE)	1.0068 (0.2637, 3.8445) 0.9920	0.9927	
Non-White	196	4 (2.0)	192 (98.0)	NE (NE, NE)	86	0	86 (100)	NE (NE, NE)	NE (NE, NE) 0.9958	0.2109	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Chills

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.5520
Asia	147	2 (1.4)	145 (98.6)	NE (NE, NE)	63	0	63 (100)	NE (NE, NE)	NE (NE, NE) 0.9970	0.3644	
North America	58	6 (10.3)	52 (89.7)	NE (NE, NE)	28	1 (3.6)	27 (96.4)	NE (NE, NE)	2.0423 (0.2430, 17.1629) 0.5109	0.5021	
Europe + Israel	166	5 (3.0)	161 (97.0)	NE (NE, NE)	81	2 (2.5)	79 (97.5)	NE (NE, NE)	0.9238 (0.1688, 5.0552) 0.9271	0.9271	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: General disorders and administration site conditions; PT: Chills

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.5237
0	199	7 (3.5)	192 (96.5)	NE (NE, NE)	95	1 (1.1)	94 (98.9)	NE (NE, NE)	2.3148 (0.2781, 19.2701) 0.4376	0.4240	
1	172	6 (3.5)	166 (96.5)	NE (NE, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	1.1248 (0.2229, 5.6752) 0.8867	0.8867	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: General disorders and administration site conditions; PT: Chills

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.4190
0	60	3 (5.0)	57 (95.0)	NE (17.9, NE)	31	0	31 (100)	NE (NE, NE)	NE (NE, NE) 0.9974	0.4680	
1	107	4 (3.7)	103 (96.3)	NE (NE, NE)	48	2 (4.2)	46 (95.8)	NE (NE, NE)	0.8589 (0.1572, 4.6938) 0.8607	0.8613	
2	114	4 (3.5)	110 (96.5)	NE (NE, NE)	50	1 (2.0)	49 (98.0)	NE (NE, NE)	1.3501 (0.1471, 12.3882) 0.7907	0.7899	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: General disorders and administration site conditions; PT: Chills

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	2 (2.2)	88 (97.8)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9969	0.3453	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Chills

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.9962
PD	173	5 (2.9)	168 (97.1)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	1.7935 (0.2083, 15.4404)	0.5897	
PR	48	0	48 (100)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	NE (NE, NE)	NE	
SD	82	6 (7.3)	76 (92.7)	NE (NE, NE)	54	2 (3.7)	52 (96.3)	NE (NE, NE)	1.4072 (0.2714, 7.2965)	0.6827	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Chills

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.0349
Yes	37	0	37 (100)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	0.0000 (0.0000, ) 0.9980	0.0916	
No	334	13 (3.9)	321 (96.1)	NE (NE, NE)	159	2 (1.3)	157 (98.7)	NE (NE, NE)	2.3691 (0.5276, 10.6380) 0.2604	0.2459	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Chills

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0330
Yes	24	0	24 (100)	NE (NE, NE)	7	1 (14.3)	6 (85.7)	NE (0.1, NE)	0.0000 (0.0000, ) 0.9983	0.0641	
No	347	13 (3.7)	334 (96.3)	NE (NE, NE)	165	2 (1.2)	163 (98.8)	NE (NE, NE)	2.3365 (0.5201, 10.4968) 0.2682	0.2542	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Chills

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.2753
Normal Function	201	8 (4.0)	193 (96.0)	NE (NE, NE)	80	2 (2.5)	78 (97.5)	NE (NE, NE)	1.0850 (0.2237, 5.2620) 0.9193	0.9188	
Mild Impairment	123	4 (3.3)	119 (96.7)	NE (NE, NE)	65	0	65 (100)	NE (NE, NE)	NE (NE, NE) 0.9955	0.1517	
Moderate Impairment	41	1 (2.4)	40 (97.6)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	0.4476 (0.0275, 7.2844) 0.5723	0.5622	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Chills

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.6343
Normal Function	170	6 (3.5)	164 (96.5)	NE (NE, NE)	88	2 (2.3)	86 (97.7)	NE (NE, NE)	1.0992 (0.2142, 5.6401) 0.9097	0.9105	
Mild Impairment	194	7 (3.6)	187 (96.4)	NE (NE, NE)	82	1 (1.2)	81 (98.8)	NE (NE, NE)	2.3964 (0.2915, 19.7009) 0.4162	0.4010	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Chills

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.8450
Yes	331	10 (3.0)	321 (97.0)	NE (NE, NE)	146	2 (1.4)	144 (98.6)	NE (NE, NE)	1.8875 (0.4110, 8.6682) 0.4140	0.4062	
No	40	3 (7.5)	37 (92.5)	NE (17.9, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	0.7966 (0.0692, 9.1664) 0.8552	0.8549	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Chills

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.9999
Positive	329	13 (4.0)	316 (96.0)	NE (NE, NE)	152	3 (2.0)	149 (98.0)	NE (NE, NE)	1.5339 (0.4308, 5.4614)	0.5054	
Negative	42	0	42 (100)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Chills

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.9999
Positive	331	13 (3.9)	318 (96.1)	NE (NE, NE)	155	3 (1.9)	152 (98.1)	NE (NE, NE)	1.5607 (0.4384, 5.5564)	0.4880	
Negative	40	0	40 (100)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE)	NE	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Mucosal inflammation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.8542
HER2 IHC 1+	214	5 (2.3)	209 (97.7)	NE (NE, NE)	100	3 (3.0)	97 (97.0)	NE (NE, NE)	0.4834 (0.1117, 2.0921) 0.3308	0.3210	
HER2 IHC 2+/ISH Negative	157	6 (3.8)	151 (96.2)	NE (NE, NE)	72	3 (4.2)	69 (95.8)	NE (NE, NE)	0.7985 (0.1966, 3.2426) 0.7530	0.7529	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: General disorders and administration site conditions; PT: Mucosal inflammation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.6833
1	220	6 (2.7)	214 (97.3)	NE (NE, NE)	94	4 (4.3)	90 (95.7)	NE (NE, NE)	0.4825 (0.1329, 1.7518) 0.2680	0.2580	
>=2	150	4 (2.7)	146 (97.3)	NE (NE, NE)	78	2 (2.6)	76 (97.4)	NE (NE, NE)	0.7325 (0.1280, 4.1907) 0.7265	0.7255	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Mucosal inflammation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.7729
Yes	233	8 (3.4)	225 (96.6)	NE (NE, NE)	112	4 (3.6)	108 (96.4)	NE (NE, NE)	0.7512 (0.2212, 2.5513) 0.6465	0.6457	
No	98	3 (3.1)	95 (96.9)	NE (NE, NE)	43	2 (4.7)	41 (95.3)	NE (NE, NE)	0.4831 (0.0795, 2.9347) 0.4293	0.4195	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Mucosal inflammation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6517
<65	289	7 (2.4)	282 (97.6)	NE (NE, NE)	126	4 (3.2)	122 (96.8)	NE (NE, NE)	0.6235 (0.1792, 2.1693) 0.4577	0.4539	
>=65	82	4 (4.9)	78 (95.1)	NE (NE, NE)	46	2 (4.3)	44 (95.7)	NE (NE, NE)	0.8046 (0.1436, 4.5096) 0.8048	0.8044	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Mucosal inflammation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0833
<75	357	9 (2.5)	348 (97.5)	NE (NE, NE)	163	6 (3.7)	157 (96.3)	NE (NE, NE)	0.4983 (0.1729, 1.4364) 0.1972	0.1889	
>=75	14	2 (14.3)	12 (85.7)	NE (4.7, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9979	0.2855	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Mucosal inflammation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.9590
White	175	9 (5.1)	166 (94.9)	NE (NE, NE)	85	5 (5.9)	80 (94.1)	NE (NE, NE)	0.7089 (0.2345, 2.1433) 0.5422	0.5405	
Non-White	196	2 (1.0)	194 (99.0)	NE (NE, NE)	86	1 (1.2)	85 (98.8)	NE (NE, NE)	0.4066 (0.0354, 4.6656) 0.4698	0.4555	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Mucosal inflammation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.5321
Asia	147	0	147 (100)	NE (NE, NE)	63	0	63 (100)	NE (NE, NE)	NE (NE, NE)		
North America	58	5 (8.6)	53 (91.4)	NE (NE, NE)	28	1 (3.6)	27 (96.4)	NE (NE, NE)	1.8348 (0.2128, 15.8210) 0.5808	0.5751	
Europe + Israel	166	6 (3.6)	160 (96.4)	NE (NE, NE)	81	5 (6.2)	76 (93.8)	NE (NE, NE)	0.4299 (0.1271, 1.4546) 0.1747	0.1633	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Mucosal inflammation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.3967
0	199	5 (2.5)	194 (97.5)	NE (NE, NE)	95	4 (4.2)	91 (95.8)	NE (NE, NE)	0.4163 (0.1087, 1.5942) 0.2008	0.1878	
1	172	6 (3.5)	166 (96.5)	NE (NE, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	1.1201 (0.2223, 5.6443) 0.8906	0.8906	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Mucosal inflammation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.9057
0	60	0	60 (100)	NE (NE, NE)	31	0	31 (100)	NE (NE, NE)	NE (NE, NE)		
1	107	4 (3.7)	103 (96.3)	NE (NE, NE)	48	2 (4.2)	46 (95.8)	NE (NE, NE)	0.7394 (0.1338, 4.0847)	0.7283	
2	114	4 (3.5)	110 (96.5)	NE (NE, NE)	50	3 (6.0)	47 (94.0)	NE (NE, NE)	0.7292 (0.0823, 1.9043)	0.2325	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Mucosal inflammation

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	3 (3.3)	87 (96.7)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	1.1442 (0.1168, 11.2126) 0.9078	0.9078

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Mucosal inflammation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.7714
PD	173	6 (3.5)	167 (96.5)	NE (NE, NE)	77	4 (5.2)	73 (94.8)	NE (NE, NE)	0.4065 (0.1082, 1.5270)	0.1695	
PR	48	1 (2.1)	47 (97.9)	NE (NE, NE)	21	1 (4.8)	20 (95.2)	NE (NE, NE)	0.1825 (0.0221, 5.6625)	0.4423	
SD	82	2 (2.4)	80 (97.6)	NE (NE, NE)	54	1 (1.9)	53 (98.1)	NE (NE, NE)	0.4624 (0.1188, 14.4579)	0.8247	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Mucosal inflammation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.1226
Yes	37	3 (8.1)	34 (91.9)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9965	0.3150	
No	334	8 (2.4)	326 (97.6)	NE (NE, NE)	159	6 (3.8)	153 (96.2)	NE (NE, NE)	0.4435 (0.1498, 1.3135) 0.1422	0.1323	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Mucosal inflammation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.4037
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.5637	
No	347	10 (2.9)	337 (97.1)	NE (NE, NE)	165	6 (3.6)	159 (96.4)	NE (NE, NE)	0.5772 (0.2053, 1.6227) 0.2973	0.2921	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Mucosal inflammation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.7011
Normal Function	201	6 (3.0)	195 (97.0)	NE (NE, NE)	80	2 (2.5)	78 (97.5)	NE (NE, NE)	0.8009 (0.1543, 4.1582) 0.7917	0.7913	
Mild Impairment	123	3 (2.4)	120 (97.6)	NE (NE, NE)	65	3 (4.6)	62 (95.4)	NE (NE, NE)	0.4119 (0.0818, 2.0741) 0.2822	0.2672	
Moderate Impairment	41	2 (4.9)	39 (95.1)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	1.0619 (0.0960, 11.7470) 0.9610	0.9610	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Mucosal inflammation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.4263
Normal Function	170	7 (4.1)	163 (95.9)	NE (NE, NE)	88	3 (3.4)	85 (96.6)	NE (NE, NE)	0.9334 (0.2369, 3.6778) 0.9216	0.9216	
Mild Impairment	194	4 (2.1)	190 (97.9)	NE (NE, NE)	82	3 (3.7)	79 (96.3)	NE (NE, NE)	0.4109 (0.0878, 1.9230) 0.2587	0.2445	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: General disorders and administration site conditions; PT: Mucosal inflammation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.9998
Yes	331	11 (3.3)	320 (96.7)	NE (NE, NE)	146	6 (4.1)	140 (95.9)	NE (NE, NE)	0.6148 (0.2238, 1.6885) 0.3453	0.3412	
No	40	0	40 (100)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Mucosal inflammation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.3323
Positive	329	10 (3.0)	319 (97.0)	NE (NE, NE)	152	6 (3.9)	146 (96.1)	NE (NE, NE)	0.5703 (0.2035, 1.5986)	0.2801	
Negative	42	1 (2.4)	41 (97.6)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	0.2856 (NE, NE) 0.9977	0.4795	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: General disorders and administration site conditions; PT: Mucosal inflammation

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.9999
Positive	331	11 (3.3)	320 (96.7)	NE (NE, NE)	155	6 (3.9)	149 (96.1)	NE (NE, NE)	0.6487 (0.2360, 1.7832)	0.3984	
Negative	40	0	40 (100)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	0.4016 (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: General disorders and administration site conditions; PT: Non-cardiac chest pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.8753
HER2 IHC 1+	214	7 (3.3)	207 (96.7)	NE (NE, NE)	100	4 (4.0)	96 (96.0)	NE (NE, NE)	0.5040 (0.1411, 1.8003) 0.2915	0.2830	
HER2 IHC 2+/ISH Negative	157	3 (1.9)	154 (98.1)	NE (NE, NE)	72	2 (2.8)	70 (97.2)	NE (NE, NE)	0.6604 (0.1103, 3.9537) 0.6495	0.6492	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.2368
1	220	4 (1.8)	216 (98.2)	NE (NE, NE)	94	4 (4.3)	90 (95.7)	NE (NE, NE)	0.3193 (0.0773, 1.3186) 0.1146	0.0970	
>=2	150	6 (4.0)	144 (96.0)	NE (NE, NE)	78	2 (2.6)	76 (97.4)	NE (NE, NE)	1.0525 (0.2027, 5.4645) 0.9515	0.9515	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.6216
Yes	233	5 (2.1)	228 (97.9)	NE (NE, NE)	112	3 (2.7)	109 (97.3)	NE (NE, NE)	0.4445 (0.0984, 2.0076) 0.2919	0.2807	
No	98	3 (3.1)	95 (96.9)	NE (NE, NE)	43	3 (7.0)	40 (93.0)	NE (NE, NE)	0.3729 (0.0748, 1.8587) 0.2288	0.2105	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3752
<65	289	7 (2.4)	282 (97.6)	NE (NE, NE)	126	5 (4.0)	121 (96.0)	NE (NE, NE)	0.3930 (0.1200, 1.2870) 0.1228	0.1110	
>=65	82	3 (3.7)	79 (96.3)	NE (NE, NE)	46	1 (2.2)	45 (97.8)	NE (NE, NE)	1.5929 (0.1657, 15.3145) 0.6868	0.6839	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9998
<75	357	10 (2.8)	347 (97.2)	NE (NE, NE)	163	6 (3.7)	157 (96.3)	NE (NE, NE)	0.5382 (0.1902, 1.5226) 0.2430	0.2363	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Non-cardiac chest pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.0819
White	175	4 (2.3)	171 (97.7)	NE (NE, NE)	85	5 (5.9)	80 (94.1)	NE (NE, NE)	0.2739 (0.0705, 1.0640) 0.0614	0.0467	
Non-White	196	6 (3.1)	190 (96.9)	NE (NE, NE)	86	1 (1.2)	85 (98.8)	NE (NE, NE)	1.9656 (0.2315, 16.6899) 0.5358	0.5282	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Non-cardiac chest pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.6482
Asia	147	3 (2.0)	144 (98.0)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (NE, NE)	1.2438 (0.1293, 11.9690) 0.8502	0.8499	
North America	58	3 (5.2)	55 (94.8)	NE (NE, NE)	28	1 (3.6)	27 (96.4)	NE (NE, NE)	0.7912 (0.0713, 8.7743) 0.8487	0.8483	
Europe + Israel	166	4 (2.4)	162 (97.6)	NE (NE, NE)	81	4 (4.9)	77 (95.1)	NE (NE, NE)	0.3183 (0.0764, 1.3265) 0.1159	0.0995	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Non-cardiac chest pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.6833
0	199	4 (2.0)	195 (98.0)	NE (NE, NE)	95	3 (3.2)	92 (96.8)	NE (NE, NE)	0.4962 (0.1096, 2.2474) 0.3632	0.3541	
1	172	6 (3.5)	166 (96.5)	NE (NE, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	0.6091 (0.1451, 2.5574) 0.4982	0.4945	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Non-cardiac chest pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1401
0	60	3 (5.0)	57 (95.0)	NE (NE, NE)	31	2 (6.5)	29 (93.5)	NE (NE, NE)	0.6305 (0.1027, 3.8718) 0.6184	0.6155	
1	107	1 (0.9)	106 (99.1)	NE (NE, NE)	48	3 (6.3)	45 (93.8)	NE (NE, NE)	0.1378 (0.0143, 1.3257) 0.0862	0.0444	
2	114	4 (3.5)	110 (96.5)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	NE (NE, NE) 0.9968	0.3479	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Non-cardiac chest pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	2 (2.2)	88 (97.8)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	0.6135 (0.0520, 7.2318) 0.6979	0.6955	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Non-cardiac chest pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.9939
PD	173	5 (2.9)	168 (97.1)	NE (NE, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	0.5554 (0.1269, 2.4306)	0.4304	
PR	48	2 (4.2)	46 (95.8)	NE (NE, NE)	21	1 (4.8)	20 (95.2)	NE (NE, NE)	0.4349 (0.0512, 6.7025)	0.6635	
SD	82	1 (1.2)	81 (98.8)	NE (NE, NE)	54	1 (1.9)	53 (98.1)	NE (NE, NE)	0.6296 (0.0393, 10.0772)	0.7414	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Non-cardiac chest pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.0444
Yes	37	4 (10.8)	33 (89.2)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9959	0.2405	
No	334	6 (1.8)	328 (98.2)	NE (NE, NE)	159	6 (3.8)	153 (96.2)	NE (NE, NE)	0.2988 (0.0923, 0.9675) 0.0439	0.0337	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: General disorders and administration site conditions; PT: Non-cardiac chest pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0876
Yes	24	3 (12.5)	21 (87.5)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9966	0.3262	
No	347	7 (2.0)	340 (98.0)	NE (NE, NE)	165	6 (3.6)	159 (96.4)	NE (NE, NE)	0.3603 (0.1165, 1.1141) 0.0763	0.0656	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: General disorders and administration site conditions; PT: Non-cardiac chest pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0073
Normal Function	201	4 (2.0)	197 (98.0)	NE (NE, NE)	80	6 (7.5)	74 (92.5)	NE (NE, NE)	0.1578 (0.0422, 0.5909) 0.0061	0.0020	
Mild Impairment	123	4 (3.3)	119 (96.7)	NE (NE, NE)	65	0	65 (100)	NE (NE, NE)	NE (NE, NE) 0.9959	0.2042	
Moderate Impairment	41	2 (4.9)	39 (95.1)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9967	0.2900	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: General disorders and administration site conditions; PT: Non-cardiac chest pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1824
Normal Function	170	9 (5.3)	161 (94.7)	NE (NE, NE)	88	4 (4.5)	84 (95.5)	NE (NE, NE)	0.8980 (0.2707, 2.9784) 0.8604	0.8603	
Mild Impairment	194	1 (0.5)	193 (99.5)	NE (NE, NE)	82	2 (2.4)	80 (97.6)	NE (NE, NE)	0.1271 (0.0106, 1.5177) 0.1030	0.0592	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Non-cardiac chest pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1724
Yes	331	10 (3.0)	321 (97.0)	NE (NE, NE)	146	5 (3.4)	141 (96.6)	NE (NE, NE)	0.6467 (0.2167, 1.9300) 0.4347	0.4321	
No	40	0	40 (100)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	0.0000 (0.0000, ) 0.9975	0.2148	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Non-cardiac chest pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.0590
Positive	329	7 (2.1)	322 (97.9)	NE (NE, NE)	152	6 (3.9)	146 (96.1)	NE (NE, NE)	0.3582 (0.1167, 1.0996)	0.0621	
Negative	42	3 (7.1)	39 (92.9)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	0.0728 (NE, NE) 0.9961	0.2226	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: General disorders and administration site conditions; PT: Non-cardiac chest pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.1539
Positive	331	8 (2.4)	323 (97.6)	NE (NE, NE)	155	6 (3.9)	149 (96.1)	NE (NE, NE)	0.4273 (0.1442, 1.2664)	0.1151	
Negative	40	2 (5.0)	38 (95.0)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	0.1251 (NE, NE) 0.9969	0.3473	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.3010
HER2 IHC 1+	214	106 (49.5)	108 (50.5)	5.7 (2.8, 17.4)	100	57 (57.0)	43 (43.0)	1.9 (1.0, 4.8)	0.6690 (0.4833, 0.9262) 0.0154	0.0150	
HER2 IHC 2+/ISH Negative	157	89 (56.7)	68 (43.3)	5.6 (2.6, 7.6)	72	35 (48.6)	37 (51.4)	4.0 (1.0, NE)	0.8065 (0.5415, 1.2013) 0.2902	0.2874	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.7198
1	220	127 (57.7)	93 (42.3)	3.2 (1.4, 5.7)	94	57 (60.6)	37 (39.4)	1.0 (0.7, 3.3)	0.6977 (0.5095, 0.9556) 0.0249	0.0242	
>=2	150	67 (44.7)	83 (55.3)	9.5 (6.1, NE)	78	35 (44.9)	43 (55.1)	4.2 (2.1, NE)	0.7054 (0.4631, 1.0746) 0.1042	0.1007	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.7555
Yes	233	122 (52.4)	111 (47.6)	4.9 (2.8, 9.0)	112	59 (52.7)	53 (47.3)	2.1 (1.0, 6.9)	0.7110 (0.5189, 0.9741) 0.0337	0.0326	
No	98	52 (53.1)	46 (46.9)	6.9 (1.8, NE)	43	25 (58.1)	18 (41.9)	2.4 (0.7, NE)	0.6705 (0.4138, 1.0867) 0.1047	0.1016	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7324
<65	289	149 (51.6)	140 (48.4)	5.7 (2.8, 16.1)	126	65 (51.6)	61 (48.4)	3.2 (1.0, 6.9)	0.7268 (0.5411, 0.9762) 0.0340	0.0336	
>=65	82	46 (56.1)	36 (43.9)	5.7 (2.8, 9.0)	46	27 (58.7)	19 (41.3)	2.1 (1.0, 4.0)	0.7313 (0.4518, 1.1838) 0.2029	0.1960	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8041
<75	357	189 (52.9)	168 (47.1)	5.7 (3.5, 9.0)	163	86 (52.8)	77 (47.2)	2.9 (1.0, 4.8)	0.7253 (0.5600, 0.9393) 0.0149	0.0145	
>=75	14	6 (42.9)	8 (57.1)	7.6 (0.7, NE)	9	6 (66.7)	3 (33.3)	2.6 (0.4, NE)	0.6333 (0.2030, 1.9755) 0.4313	0.4274	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.8245
White	175	84 (48.0)	91 (52.0)	6.9 (4.9, 18.2)	85	39 (45.9)	46 (54.1)	3.5 (1.0, NE)	0.7253 (0.4935, 1.0660) 0.1021	0.1036	
Non-White	196	111 (56.6)	85 (43.4)	3.4 (1.4, 7.0)	86	53 (61.6)	33 (38.4)	2.1 (0.9, 4.0)	0.7095 (0.5091, 0.9887) 0.0427	0.0406	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.8156
Asia	147	86 (58.5)	61 (41.5)	2.2 (1.3, 6.9)	63	40 (63.5)	23 (36.5)	1.2 (0.7, 4.0)	0.6647 (0.4541, 0.9729) 0.0356	0.0342	
North America	58	31 (53.4)	27 (46.6)	4.9 (1.4, NE)	28	13 (46.4)	15 (53.6)	4.2 (0.5, NE)	0.8040 (0.4165, 1.5521) 0.5157	0.5091	
Europe + Israel	166	78 (47.0)	88 (53.0)	6.9 (5.3, 17.4)	81	39 (48.1)	42 (51.9)	3.3 (1.9, NE)	0.7376 (0.4999, 1.0882) 0.1250	0.1258	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.4593
0	199	111 (55.8)	88 (44.2)	4.9 (2.7, 9.7)	95	54 (56.8)	41 (43.2)	2.6 (1.0, 4.0)	0.6423 (0.4604, 0.8960) 0.0091	0.0087	
1	172	84 (48.8)	88 (51.2)	6.1 (3.2, NE)	77	38 (49.4)	39 (50.6)	2.9 (0.9, NE)	0.8194 (0.5575, 1.2043) 0.3107	0.3049	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.6245
0	60	31 (51.7)	29 (48.3)	6.3 (1.4, NE)	31	15 (48.4)	16 (51.6)	2.9 (0.7, NE)	0.8340 (0.4465, 1.5578) 0.5690	0.5620	
1	107	56 (52.3)	51 (47.7)	4.6 (1.9, NE)	48	25 (52.1)	23 (47.9)	3.3 (1.1, NE)	0.8875 (0.5523, 1.4260) 0.6217	0.6198	
2	114	60 (52.6)	54 (47.4)	4.9 (2.7, 16.0)	50	27 (54.0)	23 (46.0)	2.1 (0.5, NE)	0.6411 (0.4040, 1.0174) 0.0592	0.0569	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	48 (53.3)	42 (46.7)	6.2 (1.4, 17.4)	43	25 (58.1)	18 (41.9)	1.4 (0.9, 6.9)	0.5929 (0.3604, 0.9755) 0.0396	0.0375	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.9478
PD	173	81 (46.8)	92 (53.2)	9.0 (4.6, NE)	77	36 (46.8)	41 (53.2)	4.0 (1.2, NE)	0.7539 (0.5062, 1.1228)	0.1606	
PR	48	30 (62.5)	18 (37.5)	4.2 (1.0, 6.9)	21	14 (66.7)	7 (33.3)	2.6 (0.3, 6.9)	0.6613 (0.3459, 1.2644)	0.2123	
SD	82	44 (53.7)	38 (46.3)	5.3 (1.5, NE)	54	30 (55.6)	24 (44.4)	1.2 (0.7, NE)	0.7216 (0.4511, 1.1542)	0.1709	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.9188
Yes	37	15 (40.5)	22 (59.5)	16.1 (6.3, NE)	13	5 (38.5)	8 (61.5)	4.2 (0.3, NE)	0.6641 (0.2299, 1.9188)	0.4483	
No	334	180 (53.9)	154 (46.1)	4.9 (2.8, 6.9)	159	87 (54.7)	72 (45.3)	2.1 (1.0, 4.0)	0.4496 (0.7363, 0.5685, 0.9537)	0.0197	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.2578
Yes	24	11 (45.8)	13 (54.2)	16.1 (1.0, NE)	7	5 (71.4)	2 (28.6)	0.7 (0.1, 4.2)	0.4074 (0.1352, 1.2281) 0.1107	0.0983	
No	347	184 (53.0)	163 (47.0)	5.6 (3.4, 8.2)	165	87 (52.7)	78 (47.3)	2.6 (1.1, 5.3)	0.7435 (0.5743, 0.9626) 0.0245	0.0236	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.1830
Normal Function	201	113 (56.2)	88 (43.8)	4.4 (2.1, 6.9)	80	40 (50.0)	40 (50.0)	3.3 (1.0, NE)	0.8365 (0.5802, 1.2060) 0.3389	0.3406	
Mild Impairment	123	63 (51.2)	60 (48.8)	5.6 (1.5, NE)	65	34 (52.3)	31 (47.7)	2.9 (0.9, NE)	0.7575 (0.4970, 1.1545) 0.1964	0.1936	
Moderate Impairment	41	18 (43.9)	23 (56.1)	6.9 (4.6, NE)	23	16 (69.6)	7 (30.4)	1.9 (0.6, 3.5)	0.3676 (0.1834, 0.7368) 0.0048	0.0032	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.2501
Normal Function	170	92 (54.1)	78 (45.9)	6.2 (2.8, 10.6)	88	53 (60.2)	35 (39.8)	2.4 (0.9, 4.0)	0.6268 (0.4440, 0.8850) 0.0080	0.0075	
Mild Impairment	194	100 (51.5)	94 (48.5)	4.9 (2.7, 12.7)	82	38 (46.3)	44 (53.7)	3.5 (1.0, NE)	0.8518 (0.5845, 1.2413) 0.4038	0.4019	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1146
Yes	331	172 (52.0)	159 (48.0)	5.7 (3.5, 9.0)	146	82 (56.2)	64 (43.8)	2.1 (1.0, 4.0)	0.6671 (0.5112, 0.8705) 0.0029	0.0027	
No	40	23 (57.5)	17 (42.5)	5.6 (0.7, 10.6)	26	10 (38.5)	16 (61.5)	5.3 (2.4, NE)	1.1850 (0.5523, 2.5425) 0.6630	0.6632	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.3597
Positive	329	172 (52.3)	157 (47.7)	5.7 (3.5, 9.7)	152	82 (53.9)	70 (46.1)	2.4 (1.0, 4.2)	0.6978 (0.5347, 0.9107)	0.0077	
Negative	42	23 (54.8)	19 (45.2)	6.9 (0.9, 9.5)	20	10 (50.0)	10 (50.0)	5.3 (0.5, NE)	0.8648 (0.4005, 1.8673)	0.7087	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.4147
Positive	331	174 (52.6)	157 (47.4)	5.7 (3.5, 9.7)	155	84 (54.2)	71 (45.8)	2.4 (1.0, 4.2)	0.7010 (0.5386, 0.9125)	0.0078	
Negative	40	21 (52.5)	19 (47.5)	6.9 (1.2, NE)	17	8 (47.1)	9 (52.9)	5.3 (0.5, NE)	0.8868 (0.3828, 2.0542)	0.7724	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.2938
HER2 IHC 1+	214	81 (37.9)	133 (62.1)	NE (16.0, NE)	100	36 (36.0)	64 (64.0)	NE (NE, NE)	0.9199 (0.6205, 1.3636) 0.6776	0.6806	
HER2 IHC 2+/ISH Negative	157	66 (42.0)	91 (58.0)	NE (5.6, NE)	72	21 (29.2)	51 (70.8)	NE (NE, NE)	1.2589 (0.7694, 2.0600) 0.3594	0.3567	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.4099
1	220	96 (43.6)	124 (56.4)	NE (4.9, NE)	94	37 (39.4)	57 (60.6)	NE (1.2, NE)	0.9309 (0.6366, 1.3613) 0.7120	0.7149	
>=2	150	51 (34.0)	99 (66.0)	NE (NE, NE)	78	20 (25.6)	58 (74.4)	NE (NE, NE)	1.1776 (0.7001, 1.9809) 0.5378	0.5389	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.3218
Yes	233	99 (42.5)	134 (57.5)	16.0 (5.6, NE)	112	36 (32.1)	76 (67.9)	NE (NE, NE)	1.1055 (0.7536, 1.6218) 0.6079	0.6073	
No	98	34 (34.7)	64 (65.3)	NE (NE, NE)	43	16 (37.2)	27 (62.8)	NE (0.9, NE)	0.8177 (0.4512, 1.4820) 0.5071	0.5084	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3654
<65	289	114 (39.4)	175 (60.6)	NE (NE, NE)	126	44 (34.9)	82 (65.1)	NE (NE, NE)	0.9778 (0.6900, 1.3858) 0.8998	0.9038	
>=65	82	33 (40.2)	49 (59.8)	16.0 (4.4, NE)	46	13 (28.3)	33 (71.7)	NE (NE, NE)	1.2671 (0.6650, 2.4143) 0.4717	0.4721	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1669
<75	357	142 (39.8)	215 (60.2)	NE (16.0, NE)	163	56 (34.4)	107 (65.6)	NE (NE, NE)	0.9897 (0.7256, 1.3500) 0.9480	0.9498	
>=75	14	5 (35.7)	9 (64.3)	NE (0.7, NE)	9	1 (11.1)	8 (88.9)	NE (0.4, NE)	3.5850 (0.4185, 30.7116) 0.2440	0.2129	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.9332
White	175	61 (34.9)	114 (65.1)	NE (NE, NE)	85	25 (29.4)	60 (70.6)	NE (NE, NE)	1.0056 (0.6303, 1.6043) 0.9813	0.9689	
Non-White	196	86 (43.9)	110 (56.1)	NE (4.6, NE)	86	32 (37.2)	54 (62.8)	NE (4.2, NE)	1.0431 (0.6943, 1.5671) 0.8390	0.8433	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.8989
Asia	147	67 (45.6)	80 (54.4)	NE (2.8, NE)	63	23 (36.5)	40 (63.5)	NE (1.9, NE)	1.0980 (0.6830, 1.7650) 0.6996	0.7045	
North America	58	21 (36.2)	37 (63.8)	NE (3.5, NE)	28	9 (32.1)	19 (67.9)	NE (1.0, NE)	0.8986 (0.4112, 1.9635) 0.7886	0.7896	
Europe + Israel	166	59 (35.5)	107 (64.5)	NE (16.0, NE)	81	25 (30.9)	56 (69.1)	NE (NE, NE)	1.0202 (0.6378, 1.6318) 0.9335	0.9229	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.8463
0	199	78 (39.2)	121 (60.8)	NE (16.0, NE)	95	29 (30.5)	66 (69.5)	NE (NE, NE)	1.0820 (0.7054, 1.6595) 0.7181	0.7115	
1	172	69 (40.1)	103 (59.9)	NE (5.7, NE)	77	28 (36.4)	49 (63.6)	NE (NE, NE)	1.0015 (0.6447, 1.5555) 0.9948	0.9987	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.7881
0	60	17 (28.3)	43 (71.7)	NE (NE, NE)	31	10 (32.3)	21 (67.7)	NE (1.8, NE)	0.7994 (0.3653, 1.7494) 0.5753	0.5572	
1	107	47 (43.9)	60 (56.1)	NE (3.0, NE)	48	16 (33.3)	32 (66.7)	NE (NE, NE)	1.2054 (0.6834, 2.1264) 0.5188	0.5141	
2	114	45 (39.5)	69 (60.5)	NE (4.4, NE)	50	17 (34.0)	33 (66.0)	NE (NE, NE)	0.9509 (0.5432, 1.6643) 0.8600	0.8598	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	38 (42.2)	52 (57.8)	NE (6.2, NE)	43	14 (32.6)	29 (67.4)	NE (4.2, NE)	1.1402 (0.6151, 2.1134) 0.6770	0.6696	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.9738
PD	173	62 (35.8)	111 (64.2)	NE (16.0, NE)	77	24 (31.2)	53 (68.8)	NE (NE, NE)	0.9942 (0.6191, 1.5963)	0.9791	
PR	48	19 (39.6)	29 (60.4)	NE (4.2, NE)	21	6 (28.6)	15 (71.4)	NE (1.0, NE)	1.0857 (0.4324, 2.7265)	0.8623	
SD	82	34 (41.5)	48 (58.5)	NE (3.5, NE)	54	20 (37.0)	34 (63.0)	NE (1.9, NE)	0.9920 (0.5702, 1.7258)	0.9761	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.1732
Yes	37	7 (18.9)	30 (81.1)	NE (NE, NE)	13	4 (30.8)	9 (69.2)	NE (0.4, NE)	0.4253 (0.1189, 1.5209)	0.1761	
No	334	140 (41.9)	194 (58.1)	NE (6.6, NE)	159	53 (33.3)	106 (66.7)	NE (NE, NE)	1.1207 (0.8164, 1.5384)	0.4774	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.1070
Yes	24	7 (29.2)	17 (70.8)	NE (6.6, NE)	7	4 (57.1)	3 (42.9)	4.2 (0.4, 4.2)	0.3338 (0.0927, 1.2014) 0.0931	0.0780	
No	347	140 (40.3)	207 (59.7)	NE (16.0, NE)	165	53 (32.1)	112 (67.9)	NE (NE, NE)	1.1068 (0.8062, 1.5195) 0.5302	0.5290	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.6358
Normal Function	201	85 (42.3)	116 (57.7)	NE (5.7, NE)	80	27 (33.8)	53 (66.3)	NE (NE, NE)	1.1105 (0.7191, 1.7149) 0.6364	0.6307	
Mild Impairment	123	47 (38.2)	76 (61.8)	NE (5.6, NE)	65	19 (29.2)	46 (70.8)	NE (NE, NE)	1.1382 (0.6668, 1.9430) 0.6351	0.6364	
Moderate Impairment	41	14 (34.1)	27 (65.9)	NE (6.3, NE)	23	9 (39.1)	14 (60.9)	NE (0.8, NE)	0.7042 (0.3045, 1.6286) 0.4124	0.4111	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.3867
Normal Function	170	71 (41.8)	99 (58.2)	NE (6.9, NE)	88	33 (37.5)	55 (62.5)	NE (NE, NE)	0.9231 (0.6097, 1.3974) 0.7051	0.7091	
Mild Impairment	194	74 (38.1)	120 (61.9)	NE (6.6, NE)	82	23 (28.0)	59 (72.0)	NE (NE, NE)	1.2440 (0.7782, 1.9885) 0.3617	0.3621	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1007
Yes	331	130 (39.3)	201 (60.7)	NE (16.0, NE)	146	52 (35.6)	94 (64.4)	NE (NE, NE)	0.9418 (0.6822, 1.3002) 0.7156	0.7177	
No	40	17 (42.5)	23 (57.5)	NE (1.4, NE)	26	5 (19.2)	21 (80.8)	NE (NE, NE)	2.2031 (0.8105, 5.9887) 0.1216	0.1118	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.6077
Positive	329	132 (40.1)	197 (59.9)	NE (16.0, NE)	152	51 (33.6)	101 (66.4)	NE (NE, NE)	1.0086 (0.7294, 1.3947)	0.9546	
Negative	42	15 (35.7)	27 (64.3)	NE (2.3, NE)	20	6 (30.0)	14 (70.0)	NE (1.8, NE)	1.3518 (0.5233, 3.4920)	0.5382	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.7192
Positive	331	133 (40.2)	198 (59.8)	NE (16.0, NE)	155	52 (33.5)	103 (66.5)	NE (NE, NE)	1.0216 (0.7408, 1.4090)	0.8913	
Negative	40	14 (35.0)	26 (65.0)	NE (2.8, NE)	17	5 (29.4)	12 (70.6)	NE (1.8, NE)	1.2577 (0.4509, 3.5081)	0.6712	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Rash

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.5297
HER2 IHC 1+	214	16 (7.5)	198 (92.5)	NE (NE, NE)	100	7 (7.0)	93 (93.0)	NE (NE, NE)	0.7220 (0.2882, 1.8086) 0.4869	0.4853	
HER2 IHC 2+/ISH Negative	157	8 (5.1)	149 (94.9)	NE (NE, NE)	72	2 (2.8)	70 (97.2)	NE (NE, NE)	1.0743 (0.2199, 5.2485) 0.9294	0.9294	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Rash

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.2997
1	220	15 (6.8)	205 (93.2)	NE (NE, NE)	94	7 (7.4)	87 (92.6)	NE (NE, NE)	0.6725 (0.2695, 1.6783) 0.3952	0.3934	
>=2	150	9 (6.0)	141 (94.0)	NE (NE, NE)	78	2 (2.6)	76 (97.4)	NE (NE, NE)	1.2199 (0.2523, 5.8979) 0.8047	0.8044	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Rash

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.2742
Yes	233	15 (6.4)	218 (93.6)	NE (NE, NE)	112	7 (6.3)	105 (93.8)	NE (NE, NE)	0.6315 (0.2483, 1.6061) 0.3345	0.3316	
No	98	7 (7.1)	91 (92.9)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	2.1145 (0.2532, 17.6590) 0.4893	0.4783	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Rash

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3055
<65	289	19 (6.6)	270 (93.4)	NE (NE, NE)	126	8 (6.3)	118 (93.7)	NE (NE, NE)	0.6138 (0.2603, 1.4470) 0.2646	0.2607	
>=65	82	5 (6.1)	77 (93.9)	NE (NE, NE)	46	1 (2.2)	45 (97.8)	NE (NE, NE)	2.4086 (0.2796, 20.7471) 0.4236	0.4089	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Rash

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9999
<75	357	24 (6.7)	333 (93.3)	NE (NE, NE)	163	9 (5.5)	154 (94.5)	NE (NE, NE)	0.7701 (0.3492, 1.6980)	0.5167	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE)	NE	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Rash

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.8119
White	175	9 (5.1)	166 (94.9)	NE (NE, NE)	85	3 (3.5)	82 (96.5)	NE (NE, NE)	0.8168 (0.2093, 3.1874) 0.7709	0.7720	
Non-White	196	15 (7.7)	181 (92.3)	NE (NE, NE)	86	6 (7.0)	80 (93.0)	NE (NE, NE)	0.7876 (0.3000, 2.0674) 0.6277	0.6272	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Rash

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.9711
Asia	147	10 (6.8)	137 (93.2)	NE (NE, NE)	63	4 (6.3)	59 (93.7)	NE (NE, NE)	0.7374 (0.2257, 2.4091) 0.6141	0.6132	
North America	58	6 (10.3)	52 (89.7)	NE (NE, NE)	28	2 (7.1)	26 (92.9)	NE (NE, NE)	0.8944 (0.1637, 4.8876) 0.8975	0.8974	
Europe + Israel	166	8 (4.8)	158 (95.2)	NE (NE, NE)	81	3 (3.7)	78 (96.3)	NE (NE, NE)	0.7353 (0.1861, 2.9055) 0.6609	0.6599	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Skin and subcutaneous tissue disorders; PT: Rash

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.6692
0	199	17 (8.5)	182 (91.5)	NE (NE, NE)	95	7 (7.4)	88 (92.6)	NE (NE, NE)	0.7037 (0.2848, 1.7386) 0.4464	0.4452	
1	172	7 (4.1)	165 (95.9)	NE (NE, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	1.1802 (0.2375, 5.8653) 0.8395	0.8393	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Rash

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.6417
0	60	5 (8.3)	55 (91.7)	NE (NE, NE)	31	1 (3.2)	30 (96.8)	NE (5.7, NE)	1.6952 (0.1898, 15.1372) 0.6366	0.6329	
1	107	7 (6.5)	100 (93.5)	NE (NE, NE)	48	5 (10.4)	43 (89.6)	NE (NE, NE)	0.4988 (0.1567, 1.5880) 0.2391	0.2312	
2	114	7 (6.1)	107 (93.9)	NE (NE, NE)	50	2 (4.0)	48 (96.0)	NE (NE, NE)	1.0811 (0.2145, 5.4496) 0.9247	0.9239	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Rash

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	5 (5.6)	85 (94.4)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	0.9578 (0.1007, 9.1105) 0.9701	0.9704	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Rash

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.7362
PD	173	9 (5.2)	164 (94.8)	NE (NE, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	0.8611 (0.2246, 3.3017)	0.8272	
PR	48	5 (10.4)	43 (89.6)	NE (NE, NE)	21	2 (9.5)	19 (90.5)	NE (5.7, NE)	0.7985 (0.1496, 4.2614)	0.7919	
SD	82	7 (8.5)	75 (91.5)	NE (NE, NE)	54	2 (3.7)	52 (96.3)	NE (NE, NE)	1.4459 (0.2901, 7.2055)	0.6509	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Rash

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.3077
Yes	37	2 (5.4)	35 (94.6)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9971	0.4047	
No	334	22 (6.6)	312 (93.4)	NE (NE, NE)	159	9 (5.7)	150 (94.3)	NE (NE, NE)	(0.3272, 1.6203) 0.4368	0.4357	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Rash

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.2964
Yes	24	2 (8.3)	22 (91.7)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9973	0.4401	
No	347	22 (6.3)	325 (93.7)	NE (NE, NE)	165	9 (5.5)	156 (94.5)	NE (NE, NE)	0.7153 (0.3211, 1.5933) 0.4123	0.4108	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Rash

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.5484
Normal Function	201	14 (7.0)	187 (93.0)	NE (NE, NE)	80	6 (7.5)	74 (92.5)	NE (NE, NE)	0.5106 (0.1876, 1.3896) 0.1882	0.1810	
Mild Impairment	123	9 (7.3)	114 (92.7)	NE (NE, NE)	65	2 (3.1)	63 (96.9)	NE (NE, NE)	1.6520 (0.3463, 7.8806) 0.5289	0.5248	
Moderate Impairment	41	1 (2.4)	40 (97.6)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	0.5360 (0.0335, 8.5760) 0.6594	0.6542	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Rash

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.2887
Normal Function	170	11 (6.5)	159 (93.5)	NE (NE, NE)	88	3 (3.4)	85 (96.6)	NE (NE, NE)	1.2097 (0.3280, 4.4618) 0.7750	0.7747	
Mild Impairment	194	12 (6.2)	182 (93.8)	NE (NE, NE)	82	6 (7.3)	76 (92.7)	NE (NE, NE)	0.5095 (0.1829, 1.4194) 0.1971	0.1902	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Rash

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.8942
Yes	331	22 (6.6)	309 (93.4)	NE (NE, NE)	146	8 (5.5)	138 (94.5)	NE (NE, NE)	0.8445 (0.3693, 1.9311) 0.6888	0.6892	
No	40	2 (5.0)	38 (95.0)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (5.7, NE)	0.3705 (0.0297, 4.6253) 0.4408	0.4239	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Rash

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.8518
Positive	329	22 (6.7)	307 (93.3)	NE (NE, NE)	152	8 (5.3)	144 (94.7)	NE (NE, NE)	0.8300 (0.3616, 1.9051)	0.6605	
Negative	42	2 (4.8)	40 (95.2)	NE (NE, NE)	20	1 (5.0)	19 (95.0)	NE (5.7, NE)	0.5918 (0.0516, 6.7874)	0.6702	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Rash

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.7646
Positive	331	22 (6.6)	309 (93.4)	NE (NE, NE)	155	8 (5.2)	147 (94.8)	NE (NE, NE)	0.8408 (0.3661, 1.9309)	0.6831	
Negative	40	2 (5.0)	38 (95.0)	NE (NE, NE)	17	1 (5.9)	16 (94.1)	NE (5.7, NE)	0.4801 (0.0411, 5.6039)	0.5504	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Dry skin

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.7923
HER2 IHC 1+	214	9 (4.2)	205 (95.8)	NE (NE, NE)	100	2 (2.0)	98 (98.0)	NE (NE, NE)	1.4883 (0.3150, 7.0319) 0.6158	0.6132	
HER2 IHC 2+/ISH Negative	157	7 (4.5)	150 (95.5)	NE (NE, NE)	72	2 (2.8)	70 (97.2)	NE (NE, NE)	1.0386 (0.2088, 5.1663) 0.9631	0.9636	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Dry skin

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.5166
1	220	9 (4.1)	211 (95.9)	NE (NE, NE)	94	3 (3.2)	91 (96.8)	NE (NE, NE)	1.0250 (0.2751, 3.8194) 0.9706	0.9706	
>=2	150	6 (4.0)	144 (96.0)	NE (NE, NE)	78	1 (1.3)	77 (98.7)	NE (NE, NE)	1.8210 (0.2106, 15.7444) 0.5860	0.5808	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Dry skin

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.1126
Yes	233	9 (3.9)	224 (96.1)	NE (NE, NE)	112	4 (3.6)	108 (96.4)	NE (NE, NE)	0.6911 (0.2046, 2.3347) 0.5519	0.5495	
No	98	4 (4.1)	94 (95.9)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9962	0.2803	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Dry skin

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5681
<65	289	12 (4.2)	277 (95.8)	NE (NE, NE)	126	2 (1.6)	124 (98.4)	NE (NE, NE)	1.6195 (0.3535, 7.4197) 0.5347	0.5311	
>=65	82	4 (4.9)	78 (95.1)	NE (NE, NE)	46	2 (4.3)	44 (95.7)	NE (NE, NE)	0.9234 (0.1672, 5.0999) 0.9272	0.9272	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Dry skin

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3548
<75	357	15 (4.2)	342 (95.8)	NE (NE, NE)	163	4 (2.5)	159 (97.5)	NE (NE, NE)	1.1057 (0.3585, 3.4105) 0.8612	0.8612	
>=75	14	1 (7.1)	13 (92.9)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9984	0.4054	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Dry skin

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.8134
White	175	11 (6.3)	164 (93.7)	NE (NE, NE)	85	3 (3.5)	82 (96.5)	NE (NE, NE)	1.1286 (0.3051, 4.1745) 0.8562	0.8567	
Non-White	196	5 (2.6)	191 (97.4)	NE (NE, NE)	86	1 (1.2)	85 (98.8)	NE (NE, NE)	1.5872 (0.1814, 13.8873) 0.6763	0.6737	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Dry skin

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.0139
Asia	147	5 (3.4)	142 (96.6)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (NE, NE)	1.5294 (0.1746, 13.3973) 0.7012	0.6992	
North America	58	2 (3.4)	56 (96.6)	NE (18.2, NE)	28	3 (10.7)	25 (89.3)	NE (NE, NE)	0.0876 (0.0079, 0.9693) 0.0471	0.0176	
Europe + Israel	166	9 (5.4)	157 (94.6)	NE (NE, NE)	81	0	81 (100)	NE (NE, NE)	NE (NE, NE) 0.9939	0.0699	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Dry skin

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.8208
0	199	9 (4.5)	190 (95.5)	NE (NE, NE)	95	2 (2.1)	93 (97.9)	NE (NE, NE)	1.4088 (0.2948, 6.7325) 0.6676	0.6659	
1	172	7 (4.1)	165 (95.9)	NE (NE, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	1.1127 (0.2266, 5.4636) 0.8954	0.8953	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Dry skin

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.2191
0	60	4 (6.7)	56 (93.3)	NE (NE, NE)	31	0	31 (100)	NE (NE, NE)	NE (NE, NE) 0.9959	0.2230	
1	107	6 (5.6)	101 (94.4)	NE (NE, NE)	48	1 (2.1)	47 (97.9)	NE (NE, NE)	1.8607 (0.2160, 16.0330) 0.5720	0.5665	
2	114	2 (1.8)	112 (98.2)	NE (NE, NE)	50	2 (4.0)	48 (96.0)	NE (NE, NE)	0.3226 (0.0429, 2.4252) 0.2717	0.2489	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Dry skin

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	4 (4.4)	86 (95.6)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	1.0639 (0.1127, 10.0384) 0.9569	0.9569	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Dry skin

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.5185
PD	173	2 (1.2)	171 (98.8)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	0.5381 (0.0468, 6.1893)	0.6138	
PR	48	4 (8.3)	44 (91.7)	NE (NE, NE)	21	1 (4.8)	20 (95.2)	NE (NE, NE)	0.6190 (0.0954, 8.6331)	0.9328	
SD	82	7 (8.5)	75 (91.5)	NE (NE, NE)	54	1 (1.9)	53 (98.1)	NE (NE, NE)	0.9077 (0.5116, 34.0472)	0.1472	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Dry skin

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.5676
Yes	37	1 (2.7)	36 (97.3)	NE (18.2, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE)		
No	334	15 (4.5)	319 (95.5)	NE (NE, NE)	159	4 (2.5)	155 (97.5)	NE (NE, NE)	1.2894 (0.4223, 3.9368)	0.6544	0.6553

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Dry skin

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.9999
Yes	24	0	24 (100)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE)		
No	347	16 (4.6)	331 (95.4)	NE (NE, NE)	165	4 (2.4)	161 (97.6)	NE (NE, NE)	1.2794 (0.4194, 3.9033) 0.6651	0.6642	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Dry skin

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0720
Normal Function	201	10 (5.0)	191 (95.0)	NE (NE, NE)	80	0	80 (100)	NE (NE, NE)	NE (NE, NE) 0.9945	0.1275	
Mild Impairment	123	3 (2.4)	120 (97.6)	NE (NE, NE)	65	2 (3.1)	63 (96.9)	NE (NE, NE)	0.7063 (0.1178, 4.2341) 0.7036	0.7022	
Moderate Impairment	41	3 (7.3)	38 (92.7)	NE (NE, NE)	23	2 (8.7)	21 (91.3)	NE (NE, NE)	0.7289 (0.1215, 4.3740) 0.7294	0.7284	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Dry skin

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.8470
Normal Function	170	8 (4.7)	162 (95.3)	NE (NE, NE)	88	2 (2.3)	86 (97.7)	NE (NE, NE)	1.3405 (0.2757, 6.5176) 0.7164	0.7154	
Mild Impairment	194	8 (4.1)	186 (95.9)	NE (NE, NE)	82	2 (2.4)	80 (97.6)	NE (NE, NE)	1.1928 (0.2483, 5.7301) 0.8258	0.8250	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Dry skin

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.6000
Yes	331	14 (4.2)	317 (95.8)	NE (NE, NE)	146	3 (2.1)	143 (97.9)	NE (NE, NE)	1.3415 (0.3785, 4.7545) 0.6491	0.6478	
No	40	2 (5.0)	38 (95.0)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	1.2884 (0.1168, 14.2102) 0.8361	0.8357	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Dry skin

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.2140
Positive	329	13 (4.0)	316 (96.0)	NE (NE, NE)	152	4 (2.6)	148 (97.4)	NE (NE, NE)	0.9637 (0.3063, 3.0317)	0.9499	
Negative	42	3 (7.1)	39 (92.9)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) 0.9962	0.2402	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Dry skin

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.2461
Positive	331	13 (3.9)	318 (96.1)	NE (NE, NE)	155	4 (2.6)	151 (97.4)	NE (NE, NE)	0.9777 (0.3107, 3.0769)	0.9693	
Negative	40	3 (7.5)	37 (92.5)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) 0.9964	0.2893	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Pruritus

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.9199
HER2 IHC 1+	214	7 (3.3)	207 (96.7)	NE (NE, NE)	100	4 (4.0)	96 (96.0)	NE (NE, NE)	0.4494 (0.1229, 1.6428) 0.2265	0.2162	
HER2 IHC 2+/ISH Negative	157	5 (3.2)	152 (96.8)	NE (NE, NE)	72	3 (4.2)	69 (95.8)	NE (NE, NE)	0.5322 (0.1172, 2.4166) 0.4140	0.4067	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Pruritus

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.9039
1	220	8 (3.6)	212 (96.4)	NE (NE, NE)	94	5 (5.3)	89 (94.7)	NE (NE, NE)	0.4425 (0.1374, 1.4251) 0.1718	0.1615	
>=2	150	3 (2.0)	147 (98.0)	NE (NE, NE)	78	2 (2.6)	76 (97.4)	NE (NE, NE)	0.5467 (0.0874, 3.4201) 0.5186	0.5132	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Skin and subcutaneous tissue disorders; PT: Pruritus

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.3561
Yes	233	6 (2.6)	227 (97.4)	NE (NE, NE)	112	4 (3.6)	108 (96.4)	NE (NE, NE)	0.3692 (0.0930, 1.4656) 0.1566	0.1425	
No	98	5 (5.1)	93 (94.9)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	1.6593 (0.1886, 14.6000) 0.6481	0.6447	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Skin and subcutaneous tissue disorders; PT: Pruritus

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3810
<65	289	9 (3.1)	280 (96.9)	NE (NE, NE)	126	6 (4.8)	120 (95.2)	NE (NE, NE)	0.4337 (0.1456, 1.2921) 0.1336	0.1233	
>=65	82	3 (3.7)	79 (96.3)	NE (NE, NE)	46	1 (2.2)	45 (97.8)	NE (NE, NE)	0.8772 (0.0862, 8.9312) 0.9119	0.9118	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Skin and subcutaneous tissue disorders; PT: Pruritus

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9997
<75	357	12 (3.4)	345 (96.6)	NE (NE, NE)	163	7 (4.3)	156 (95.7)	NE (NE, NE)	0.4692 (0.1745, 1.2613)	0.1254	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE)	NE	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Pruritus

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.7771
White	175	4 (2.3)	171 (97.7)	NE (NE, NE)	85	2 (2.4)	83 (97.6)	NE (NE, NE)	0.4506 (0.0691, 2.9398) 0.4048	0.3942	
Non-White	196	8 (4.1)	188 (95.9)	NE (NE, NE)	86	5 (5.8)	81 (94.2)	NE (NE, NE)	0.4872 (0.1533, 1.5484) 0.2229	0.2140	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Pruritus

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.8593
Asia	147	6 (4.1)	141 (95.9)	NE (NE, NE)	63	4 (6.3)	59 (93.7)	NE (NE, NE)	0.4551 (0.1223, 1.6933) 0.2403	0.2294	
North America	58	3 (5.2)	55 (94.8)	NE (18.4, NE)	28	1 (3.6)	27 (96.4)	NE (NE, NE)	0.4870 (0.0305, 7.7861) 0.6109	0.6032	
Europe + Israel	166	3 (1.8)	163 (98.2)	NE (NE, NE)	81	2 (2.5)	79 (97.5)	NE (NE, NE)	0.4616 (0.0737, 2.8904) 0.4088	0.3983	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Skin and subcutaneous tissue disorders; PT: Pruritus

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.1915
0	199	7 (3.5)	192 (96.5)	NE (NE, NE)	95	6 (6.3)	89 (93.7)	NE (NE, NE)	0.3177 (0.0988, 1.0217) 0.0544	0.0436	
1	172	5 (2.9)	167 (97.1)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	1.5708 (0.1741, 14.1728) 0.6874	0.6850	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Pruritus

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.4970
0	60	3 (5.0)	57 (95.0)	NE (NE, NE)	31	3 (9.7)	28 (90.3)	NE (5.3, NE)	0.4467 (0.0884, 2.2576) 0.3296	0.3172	
1	107	5 (4.7)	102 (95.3)	NE (NE, NE)	48	1 (2.1)	47 (97.9)	NE (NE, NE)	1.5857 (0.1757, 14.3129) 0.6813	0.6787	
2	114	3 (2.6)	111 (97.4)	NE (NE, NE)	50	2 (4.0)	48 (96.0)	NE (NE, NE)	0.1994 (0.0244, 1.6291) 0.1324	0.1060	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Skin and subcutaneous tissue disorders; PT: Pruritus

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	1 (1.1)	89 (98.9)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	0.1995 (0.0095, 4.1721) 0.2988	0.2652	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.8785
PD	173	5 (2.9)	168 (97.1)	NE (NE, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	0.5861 (0.1351, 2.5421)	0.4707	
PR	48	1 (2.1)	47 (97.9)	NE (NE, NE)	21	1 (4.8)	20 (95.2)	NE (5.3, NE)	0.2635 (0.0153, 4.5323)	0.3271	
SD	82	4 (4.9)	78 (95.1)	NE (NE, NE)	54	3 (5.6)	51 (94.4)	NE (NE, NE)	0.5632 (0.1192, 2.6601)	0.4635	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.5744
Yes	37	1 (2.7)	36 (97.3)	NE (18.4, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	0.0000 (0.0000, )	0.0916	
No	334	11 (3.3)	323 (96.7)	NE (NE, NE)	159	6 (3.8)	153 (96.2)	NE (NE, NE)	0.5811 (0.2073, 1.6289)	0.2968	

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 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.1146
Yes	24	0	24 (100)	NE (NE, NE)	7	1 (14.3)	6 (85.7)	NE (0.3, NE)	0.0000 (0.0000, ) 0.9983	0.0641	
No	347	12 (3.5)	335 (96.5)	NE (NE, NE)	165	6 (3.6)	159 (96.4)	NE (NE, NE)	0.5748 (0.2048, 1.6132) 0.2929	0.2876	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.6489
Normal Function	201	5 (2.5)	196 (97.5)	NE (NE, NE)	80	4 (5.0)	76 (95.0)	NE (NE, NE)	0.3034 (0.0716, 1.2853) 0.1054	0.0868	
Mild Impairment	123	7 (5.7)	116 (94.3)	NE (NE, NE)	65	3 (4.6)	62 (95.4)	NE (NE, NE)	0.6665 (0.1598, 2.7796) 0.5777	0.5758	
Moderate Impairment	41	0	41 (100)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1972
Normal Function	170	6 (3.5)	164 (96.5)	NE (NE, NE)	88	6 (6.8)	82 (93.2)	NE (NE, NE)	0.2980 (0.0868, 1.0227) 0.0543	0.0425	
Mild Impairment	194	5 (2.6)	189 (97.4)	NE (NE, NE)	82	1 (1.2)	81 (98.8)	NE (NE, NE)	1.2404 (0.1370, 11.2276) 0.8480	0.8477	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Pruritus

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.9933
Yes	331	9 (2.7)	322 (97.3)	NE (NE, NE)	146	5 (3.4)	141 (96.6)	NE (NE, NE)	0.5219 (0.1652, 1.6485) 0.2678	0.2598	
No	40	3 (7.5)	37 (92.5)	NE (NE, NE)	26	2 (7.7)	24 (92.3)	NE (5.3, NE)	0.4203 (0.0609, 2.9003) 0.3791	0.3672	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Pruritus

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.2503
Positive	329	11 (3.3)	318 (96.7)	NE (NE, NE)	152	5 (3.3)	147 (96.7)	NE (NE, NE)	0.6221 (0.2053, 1.8848)	0.3977	
Negative	42	1 (2.4)	41 (97.6)	NE (NE, NE)	20	2 (10.0)	18 (90.0)	NE (5.3, NE)	0.1616 (0.0135, 1.9327)	0.1069	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Pruritus

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.2118
Positive	331	11 (3.3)	320 (96.7)	NE (NE, NE)	155	5 (3.2)	150 (96.8)	NE (NE, NE)	0.6294 (0.2076, 1.9082)	0.4098	
Negative	40	1 (2.5)	39 (97.5)	NE (NE, NE)	17	2 (11.8)	15 (88.2)	NE (5.3, NE)	0.1345 (0.0109, 1.6561)	0.0742	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Rash maculo-papular

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0484
HER2 IHC 1+	214	2 (0.9)	212 (99.1)	NE (NE, NE)	100	3 (3.0)	97 (97.0)	NE (NE, NE)	0.2872 (0.0478, 1.7250) 0.1726	0.1462	
HER2 IHC 2+/ISH Negative	157	8 (5.1)	149 (94.9)	NE (21.7, NE)	72	1 (1.4)	71 (98.6)	NE (NE, NE)	1.9822 (0.2372, 16.5635) 0.5276	0.5199	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Rash maculo-papular

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.0050
1	220	3 (1.4)	217 (98.6)	NE (NE, NE)	94	4 (4.3)	90 (95.7)	NE (NE, NE)	0.2637 (0.0578, 1.2022) 0.0851	0.0650	
>=2	150	7 (4.7)	143 (95.3)	NE (21.7, NE)	78	0	78 (100)	NE (NE, NE)	NE (NE, NE) 0.9954	0.1800	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Rash maculo-papular

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.1303
Yes	233	3 (1.3)	230 (98.7)	NE (NE, NE)	112	2 (1.8)	110 (98.2)	NE (NE, NE)	0.3914 (0.0576, 2.6611) 0.3375	0.3233	
No	98	3 (3.1)	95 (96.9)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9964	0.3008	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Rash maculo-papular

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7068
<65	289	7 (2.4)	282 (97.6)	NE (NE, NE)	126	2 (1.6)	124 (98.4)	NE (NE, NE)	1.0121 (0.2016, 5.0818) 0.9883	0.9883	
>=65	82	3 (3.7)	79 (96.3)	NE (21.7, NE)	46	2 (4.3)	44 (95.7)	NE (NE, NE)	0.4703 (0.0656, 3.3715) 0.4529	0.4424	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Rash maculo-papular

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9999
<75	357	10 (2.8)	347 (97.2)	NE (NE, NE)	163	4 (2.5)	159 (97.5)	NE (NE, NE)	0.7087 (0.2118, 2.3711) 0.5763	0.5747	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Skin and subcutaneous tissue disorders; PT: Rash maculo-papular

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.2246
White	175	4 (2.3)	171 (97.7)	NE (NE, NE)	85	3 (3.5)	82 (96.5)	NE (NE, NE)	0.5050 (0.1082, 2.3582) 0.3849	0.3764	
Non-White	196	6 (3.1)	190 (96.9)	NE (21.7, NE)	86	1 (1.2)	85 (98.8)	NE (NE, NE)	1.3696 (0.1565, 11.9847) 0.7763	0.7753	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Rash maculo-papular

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.4920
Asia	147	6 (4.1)	141 (95.9)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (NE, NE)	1.2833 (0.1468, 11.2204) 0.8216	0.8211	
North America	58	3 (5.2)	55 (94.8)	NE (NE, NE)	28	2 (7.1)	26 (92.9)	NE (NE, NE)	0.4358 (0.0613, 3.0965) 0.4064	0.3929	
Europe + Israel	166	1 (0.6)	165 (99.4)	NE (NE, NE)	81	1 (1.2)	80 (98.8)	NE (NE, NE)	0.4875 (0.0305, 7.7940) 0.6114	0.6037	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Rash maculo-papular

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.2470
0	199	6 (3.0)	193 (97.0)	NE (NE, NE)	95	1 (1.1)	94 (98.9)	NE (NE, NE)	1.4596 (0.1650, 12.9138) 0.7339	0.7322	
1	172	4 (2.3)	168 (97.7)	NE (NE, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	0.4972 (0.1084, 2.2804) 0.3685	0.3596	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Rash maculo-papular

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1442
0	60	4 (6.7)	56 (93.3)	NE (NE, NE)	31	2 (6.5)	29 (93.5)	NE (NE, NE)	0.8204 (0.1463, 4.6016) 0.8219	0.8217	
1	107	2 (1.9)	105 (98.1)	NE (NE, NE)	48	0	48 (100)	NE (NE, NE)	NE (NE, NE) 0.9972	0.4137	
2	114	1 (0.9)	113 (99.1)	NE (NE, NE)	50	2 (4.0)	48 (96.0)	NE (NE, NE)	0.0861 (0.0054, 1.3682) 0.0822	0.0448	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Rash maculo-papular

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	3 (3.3)	87 (96.7)	NE (21.7, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9961	0.4913	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Rash maculo-papular

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.6808
PD	173	6 (3.5)	167 (96.5)	NE (21.7, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	0.6242 (0.1125, 3.4645)	0.5873	
PR	48	1 (2.1)	47 (97.9)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	0.5899 (NE, NE)	0.9978	0.5083
SD	82	1 (1.2)	81 (98.8)	NE (NE, NE)	54	1 (1.9)	53 (98.1)	NE (NE, NE)	0.4411 (0.0273, 7.1219)	0.5534	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Rash maculo-papular

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.2838
Yes	37	2 (5.4)	35 (94.6)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9971	0.4047	
No	334	8 (2.4)	326 (97.6)	NE (NE, NE)	159	4 (2.5)	155 (97.5)	NE (NE, NE)	0.5415 (0.1530, 1.9163) 0.3414	0.3346	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Rash maculo-papular

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.4503
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9981	0.5892	
No	347	9 (2.6)	338 (97.4)	NE (NE, NE)	165	4 (2.4)	161 (97.6)	NE (NE, NE)	0.6370 (0.1858, 2.1835) 0.4731	0.4699	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Rash maculo-papular

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0444
Normal Function	201	4 (2.0)	197 (98.0)	NE (NE, NE)	80	0	80 (100)	NE (NE, NE)	NE (NE, NE) 0.9947	0.3286	
Mild Impairment	123	6 (4.9)	117 (95.1)	NE (21.7, NE)	65	2 (3.1)	63 (96.9)	NE (NE, NE)	0.9554 (0.1797, 5.0813) 0.9574	0.9578	
Moderate Impairment	41	0	41 (100)	NE (NE, NE)	23	2 (8.7)	21 (91.3)	NE (NE, NE)	0.0000 (0.0000, ) 0.9967	0.0478	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Rash maculo-papular

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.7248
Normal Function	170	6 (3.5)	164 (96.5)	NE (21.7, NE)	88	3 (3.4)	85 (96.6)	NE (NE, NE)	0.6541 (0.1516, 2.8219) 0.5693	0.5667	
Mild Impairment	194	4 (2.1)	190 (97.9)	NE (NE, NE)	82	1 (1.2)	81 (98.8)	NE (NE, NE)	1.0507 (0.1120, 9.8526) 0.9655	0.9655	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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SOC: Skin and subcutaneous tissue disorders; PT: Rash maculo-papular

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1419
Yes	331	9 (2.7)	322 (97.3)	NE (NE, NE)	146	2 (1.4)	144 (98.6)	NE (NE, NE)	1.4269 (0.3021, 6.7385) 0.6536	0.6517	
No	40	1 (2.5)	39 (97.5)	NE (21.7, NE)	26	2 (7.7)	24 (92.3)	NE (NE, NE)	0.0000 (0.0000, ) 0.9967	0.0435	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Rash maculo-papular

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.9105
Positive	329	5 (1.5)	324 (98.5)	NE (NE, NE)	152	2 (1.3)	150 (98.7)	NE (NE, NE)	0.7369 (0.1374, 3.9529)	0.7208	
Negative	42	5 (11.9)	37 (88.1)	21.7 (NE, NE)	20	2 (10.0)	18 (90.0)	NE (NE, NE)	0.7216 (0.1310, 4.3579)	0.7531	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Rash maculo-papular

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.7015
Positive	331	6 (1.8)	325 (98.2)	NE (NE, NE)	155	2 (1.3)	153 (98.7)	NE (NE, NE)	0.9587 (0.1874, 4.9047)	0.9596	0.9600
Negative	40	4 (10.0)	36 (90.0)	21.7 (NE, NE)	17	2 (11.8)	15 (88.2)	NE (2.9, NE)	0.4537 (0.0697, 2.9519)	0.4082	0.3970

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysesthesia syndrome

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.2438
HER2 IHC 1+	214	4 (1.9)	210 (98.1)	NE (NE, NE)	100	13 (13.0)	87 (87.0)	NE (NE, NE)	0.0997 (0.0318, 0.3128) 0.0001	<0.0001	
HER2 IHC 2+/ISH Negative	157	1 (0.6)	156 (99.4)	NE (NE, NE)	72	11 (15.3)	61 (84.7)	NE (NE, NE)	0.0356 (0.0046, 0.2762) 0.0014	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysesthesia syndrome

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.4199
1	220	4 (1.8)	216 (98.2)	NE (NE, NE)	94	14 (14.9)	80 (85.1)	NE (NE, NE)	0.0905 (0.0294, 0.2789) <0.0001	<0.0001	
>=2	150	1 (0.7)	149 (99.3)	NE (NE, NE)	78	10 (12.8)	68 (87.2)	NE (NE, NE)	0.0416 (0.0053, 0.3275) 0.0025	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysesthesia syndrome

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.5664
Yes	233	2 (0.9)	231 (99.1)	NE (NE, NE)	112	16 (14.3)	96 (85.7)	NE (NE, NE)	0.0380 (0.0084, 0.1713) <0.0001	<0.0001	
No	98	2 (2.0)	96 (98.0)	NE (NE, NE)	43	8 (18.6)	35 (81.4)	NE (NE, NE)	0.0900 (0.0190, 0.4258) 0.0024	0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysesthesia syndrome

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0357
<65	289	5 (1.7)	284 (98.3)	NE (NE, NE)	126	13 (10.3)	113 (89.7)	NE (NE, NE)	0.1175 (0.0406, 0.3399)	<0.0001	
>=65	82	0	82 (100)	NE (NE, NE)	46	11 (23.9)	35 (76.1)	NE (NE, NE)	0.0000 (0.0000, 0.9924)	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysesthesia syndrome

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3552
<75	357	5 (1.4)	352 (98.6)	NE (NE, NE)	163	21 (12.9)	142 (87.1)	NE (NE, NE)	0.0778 (0.0288, 0.2102) <0.0001	<0.0001	
>=75	14	0	14 (100)	NE (NE, NE)	9	3 (33.3)	6 (66.7)	NE (0.6, NE)	0.0000 (0.0000, ) 0.9973	0.0268	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysesthesia syndrome

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Race									0.5135	
White	175	3 (1.7)	172 (98.3)	NE (NE, NE)	85	11 (12.9)	74 (87.1)	NE (NE, NE)	0.0994 (0.0272, 0.3637) 0.0005	<0.0001
Non-White	196	2 (1.0)	194 (99.0)	NE (NE, NE)	86	13 (15.1)	73 (84.9)	NE (NE, NE)	0.0496 (0.0110, 0.2245) 0.0001	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysesthesia syndrome

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.4119
Asia	147	1 (0.7)	146 (99.3)	NE (NE, NE)	63	11 (17.5)	52 (82.5)	NE (6.9, NE)	0.0274 (0.0035, 0.2171) 0.0007	<0.0001	
North America	58	1 (1.7)	57 (98.3)	NE (NE, NE)	28	4 (14.3)	24 (85.7)	NE (NE, NE)	0.0579 (0.0055, 0.6075) 0.0175	0.0027	
Europe + Israel	166	3 (1.8)	163 (98.2)	NE (NE, NE)	81	9 (11.1)	72 (88.9)	NE (NE, NE)	0.1393 (0.0376, 0.5168) 0.0032	0.0006	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysesthesia syndrome

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.5874
0	199	3 (1.5)	196 (98.5)	NE (NE, NE)	95	17 (17.9)	78 (82.1)	NE (NE, NE)	0.0518 (0.0148, 0.1808) <0.0001	<0.0001	
1	172	2 (1.2)	170 (98.8)	NE (NE, NE)	77	7 (9.1)	70 (90.9)	NE (NE, NE)	0.1236 (0.0257, 0.5954) 0.0091	0.0019	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysesthesia syndrome

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.0390
0	60	2 (3.3)	58 (96.7)	NE (NE, NE)	31	1 (3.2)	30 (96.8)	NE (NE, NE)	1.0278 (0.0932, 11.3354) 0.9821	0.9821	
1	107	2 (1.9)	105 (98.1)	NE (NE, NE)	48	7 (14.6)	41 (85.4)	NE (NE, NE)	0.1084 (0.0225, 0.5231) 0.0057	0.0008	
2	114	1 (0.9)	113 (99.1)	NE (NE, NE)	50	7 (14.0)	43 (86.0)	NE (NE, NE)	0.0385 (0.0045, 0.3331) 0.0031	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysesthesia syndrome

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	0	90 (100)	NE (NE, NE)	43	9 (20.9)	34 (79.1)	NE (6.9, NE)	0.0000 (0.0000, ) 0.9933	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysesthesia syndrome

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.4759
PD	173	3 (1.7)	170 (98.3)	NE (NE, NE)	77	5 (6.5)	72 (93.5)	NE (NE, NE)	0.1956 (0.0453, 0.8451)	0.0158	
PR	48	1 (2.1)	47 (97.9)	NE (NE, NE)	21	3 (14.3)	18 (85.7)	6.9 (6.9, NE)	0.0639 (0.0056, 0.7250)	0.0056	
SD	82	1 (1.2)	81 (98.8)	NE (NE, NE)	54	10 (18.5)	44 (81.5)	NE (NE, NE)	0.0603 (0.0077, 0.4716)	0.0003	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysesthesia syndrome

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											NE
Yes	37	0	37 (100)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE)	NE	
No	334	5 (1.5)	329 (98.5)	NE (NE, NE)	159	24 (15.1)	135 (84.9)	NE (NE, NE)	0.0728 (0.0273, 0.1938)	<0.0001	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysesthesia syndrome

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											NE
Yes	24	0	24 (100)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE)		
No	347	5 (1.4)	342 (98.6)	NE (NE, NE)	165	24 (14.5)	141 (85.5)	NE (NE, NE)	0.0719 (0.0270, 0.1916) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysesthesia syndrome

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.9157
Normal Function	201	2 (1.0)	199 (99.0)	NE (NE, NE)	80	7 (8.8)	73 (91.3)	NE (NE, NE)	0.0778 (0.0155, 0.3914) 0.0019	<0.0001	
Mild Impairment	123	2 (1.6)	121 (98.4)	NE (NE, NE)	65	9 (13.8)	56 (86.2)	NE (NE, NE)	0.1054 (0.0227, 0.4887) 0.0040	0.0004	
Moderate Impairment	41	1 (2.4)	40 (97.6)	NE (NE, NE)	23	8 (34.8)	15 (65.2)	NE (2.1, NE)	0.0479 (0.0059, 0.3864) 0.0043	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysesthesia syndrome

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.0356
Normal Function	170	0	170 (100)	NE (NE, NE)	88	11 (12.5)	77 (87.5)	NE (NE, NE)	0.0000 (0.0000, ) 0.9927	<0.0001	
Mild Impairment	194	5 (2.6)	189 (97.4)	NE (NE, NE)	82	13 (15.9)	69 (84.1)	NE (NE, NE)	0.1174 (0.0409, 0.3367) 0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysesthesia syndrome

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.2388
Yes	331	5 (1.5)	326 (98.5)	NE (NE, NE)	146	20 (13.7)	126 (86.3)	NE (NE, NE)	0.0829 (0.0307, 0.2238) <0.0001	<0.0001	
No	40	0	40 (100)	NE (NE, NE)	26	4 (15.4)	22 (84.6)	NE (NE, NE)	0.0000 (0.0000, ) 0.9953	0.0046	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysesthesia syndrome

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.2303
Positive	329	4 (1.2)	325 (98.8)	NE (NE, NE)	152	23 (15.1)	129 (84.9)	NE (NE, NE)	0.0572 (0.0195, 0.1678)	<0.0001	
Negative	42	1 (2.4)	41 (97.6)	NE (NE, NE)	20	1 (5.0)	19 (95.0)	NE (NE, NE)	0.4820 (0.0301, 7.7061)	0.5978	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysesthesia syndrome

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.0523
Positive	331	4 (1.2)	327 (98.8)	NE (NE, NE)	155	24 (15.5)	131 (84.5)	NE (NE, NE)	0.0559 (0.0191, 0.1636)	<0.0001	
Negative	40	1 (2.5)	39 (97.5)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) 0.9978	0.5145	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0980
HER2 IHC 1+	214	112 (52.3)	102 (47.7)	6.9 (4.2, 10.2)	100	32 (32.0)	68 (68.0)	NE (6.5, NE)	1.5357 (1.0336, 2.2816) 0.0337	0.0335	
HER2 IHC 2+/ISH Negative	157	76 (48.4)	81 (51.6)	11.7 (4.2, NE)	72	31 (43.1)	41 (56.9)	7.1 (1.6, NE)	0.9528 (0.6243, 1.4542) 0.8228	0.8196	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.3605
1	220	103 (46.8)	117 (53.2)	8.3 (5.5, NE)	94	35 (37.2)	59 (62.8)	NE (4.5, NE)	1.1254 (0.7645, 1.6566) 0.5493	0.5601	
>=2	150	84 (56.0)	66 (44.0)	5.9 (2.8, 10.2)	78	28 (35.9)	50 (64.1)	NE (6.5, NE)	1.4453 (0.9384, 2.2259) 0.0946	0.0926	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.1951
Yes	233	101 (43.3)	132 (56.7)	13.2 (7.1, NE)	112	36 (32.1)	76 (67.9)	NE (6.5, NE)	1.1463 (0.7796, 1.6856) 0.4875	0.4936	
No	98	65 (66.3)	33 (33.7)	2.9 (1.5, 6.2)	43	17 (39.5)	26 (60.5)	NE (2.0, NE)	1.7611 (1.0314, 3.0072) 0.0382	0.0368	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0564
<65	289	148 (51.2)	141 (48.8)	7.1 (4.2, 13.1)	126	39 (31.0)	87 (69.0)	NE (6.5, NE)	1.5114 (1.0588, 2.1575) 0.0229	0.0225	
>=65	82	40 (48.8)	42 (51.2)	7.8 (4.2, NE)	46	24 (52.2)	22 (47.8)	4.5 (1.0, NE)	0.8071 (0.4847, 1.3439) 0.4100	0.4110	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0189
<75	357	184 (51.5)	173 (48.5)	7.1 (4.3, 11.7)	163	56 (34.4)	107 (65.6)	NE (6.5, NE)	1.3519 (0.9997, 1.8282) 0.0502	0.0507	
>=75	14	4 (28.6)	10 (71.4)	NE (0.5, NE)	9	7 (77.8)	2 (22.2)	1.4 (0.3, 7.1)	0.3440 (0.0992, 1.1929) 0.0926	0.0820	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.4466
White	175	76 (43.4)	99 (56.6)	13.2 (7.1, NE)	85	28 (32.9)	57 (67.1)	NE (4.8, NE)	1.0784 (0.6946, 1.6743) 0.7367	0.7380	
Non-White	196	112 (57.1)	84 (42.9)	4.3 (2.8, 7.2)	86	35 (40.7)	51 (59.3)	7.1 (4.5, NE)	1.3802 (0.9425, 2.0214) 0.0978	0.1008	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.4604
Asia	147	89 (60.5)	58 (39.5)	3.7 (1.5, 6.5)	63	28 (44.4)	35 (55.6)	6.5 (2.0, NE)	1.2981 (0.8464, 1.9911) 0.2319	0.2390	
North America	58	29 (50.0)	29 (50.0)	11.8 (2.8, NE)	28	13 (46.4)	15 (53.6)	2.8 (0.7, NE)	0.8353 (0.4253, 1.6406) 0.6012	0.5979	
Europe + Israel	166	70 (42.2)	96 (57.8)	NE (7.1, NE)	81	22 (27.2)	59 (72.8)	NE (NE, NE)	1.3806 (0.8516, 2.2381) 0.1908	0.1920	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.5527
0	199	88 (44.2)	111 (55.8)	13.1 (7.6, NE)	95	25 (26.3)	70 (73.7)	NE (NE, NE)	1.3639 (0.8703, 2.1374) 0.1758	0.1735	
1	172	100 (58.1)	72 (41.9)	3.9 (1.9, 5.9)	77	38 (49.4)	39 (50.6)	4.5 (1.4, NE)	1.1974 (0.8221, 1.7440) 0.3479	0.3576	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.0285
0	60	37 (61.7)	23 (38.3)	2.1 (0.6, 11.7)	31	18 (58.1)	13 (41.9)	1.4 (0.9, NE)	0.9077 (0.5066, 1.6264) 0.7449	0.7291	
1	107	56 (52.3)	51 (47.7)	6.2 (3.6, NE)	48	20 (41.7)	28 (58.3)	NE (2.2, NE)	1.2304 (0.7371, 2.0538) 0.4278	0.4294	
2	114	55 (48.2)	59 (51.8)	7.6 (4.2, NE)	50	8 (16.0)	42 (84.0)	NE (6.5, NE)	2.9117 (1.3814, 6.1371) 0.0050	0.0033	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	40 (44.4)	50 (55.6)	11.8 (6.5, NE)	43	17 (39.5)	26 (60.5)	7.1 (2.0, NE)	0.8146 (0.4537, 1.4626) 0.4923	0.4905	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.3101
PD	173	83 (48.0)	90 (52.0)	6.9 (4.2, NE)	77	25 (32.5)	52 (67.5)	NE (6.5, NE)	1.3041 (0.8313, 2.0457) 0.2477	0.2474	
PR	48	27 (56.3)	21 (43.8)	7.5 (2.8, 14.5)	21	5 (23.8)	16 (76.2)	NE (NE, NE)	2.0608 (0.7870, 5.3966) 0.1409	0.1337	
SD	82	38 (46.3)	44 (53.7)	12.0 (4.1, NE)	54	23 (42.6)	31 (57.4)	NE (2.3, NE)	1.0329 (0.6124, 1.7422) 0.9033	0.9168	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.9472
Yes	37	20 (54.1)	17 (45.9)	4.1 (0.5, NE)	13	5 (38.5)	8 (61.5)	NE (0.2, NE)	1.3355 (0.4974, 3.5862)	0.5659	
No	334	168 (50.3)	166 (49.7)	7.5 (5.5, 12.0)	159	58 (36.5)	101 (63.5)	NE (6.5, NE)	1.2298 (0.9098, 1.6625)	0.1786	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.6952
Yes	24	14 (58.3)	10 (41.7)	1.5 (0.1, NE)	7	4 (57.1)	3 (42.9)	1.0 (0.1, NE)	1.0369 (0.3397, 3.1657) 0.9492	0.9498	
No	347	174 (50.1)	173 (49.9)	7.6 (5.5, 12.0)	165	59 (35.8)	106 (64.2)	NE (6.5, NE)	1.2428 (0.9223, 1.6748) 0.1532	0.1557	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.4224
Normal Function	201	105 (52.2)	96 (47.8)	6.3 (4.2, 11.7)	80	28 (35.0)	52 (65.0)	NE (6.5, NE)	1.3080 (0.8580, 1.9941) 0.2120	0.2135	
Mild Impairment	123	62 (50.4)	61 (49.6)	7.2 (3.7, NE)	65	24 (36.9)	41 (63.1)	NE (3.0, NE)	1.2329 (0.7653, 1.9861) 0.3895	0.3971	
Moderate Impairment	41	17 (41.5)	24 (58.5)	NE (2.9, NE)	23	11 (47.8)	12 (52.2)	7.1 (0.6, NE)	0.7845 (0.3669, 1.6775) 0.5313	0.5252	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.6994
Normal Function	170	83 (48.8)	87 (51.2)	11.7 (6.2, 14.5)	88	33 (37.5)	55 (62.5)	NE (4.8, NE)	1.0997 (0.7312, 1.6537) 0.6481	0.6593	
Mild Impairment	194	100 (51.5)	94 (48.5)	6.2 (3.5, 19.6)	82	30 (36.6)	52 (63.4)	NE (3.0, NE)	1.3129 (0.8701, 1.9810) 0.1947	0.1973	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.2527
Yes	331	160 (48.3)	171 (51.7)	8.0 (6.2, 14.5)	146	54 (37.0)	92 (63.0)	NE (6.5, NE)	1.1802 (0.8646, 1.6110) 0.2968	0.3029	
No	40	28 (70.0)	12 (30.0)	2.3 (1.3, 6.5)	26	9 (34.6)	17 (65.4)	NE (2.2, NE)	1.8471 (0.8633, 3.9517) 0.1138	0.1099	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.3106
Positive	329	165 (50.2)	164 (49.8)	7.5 (5.0, 13.1)	152	52 (34.2)	100 (65.8)	NE (7.1, NE)	1.3178 (0.9625, 1.8044) 0.0852	0.0861	
Negative	42	23 (54.8)	19 (45.2)	5.9 (0.5, NE)	20	11 (55.0)	9 (45.0)	2.4 (0.3, NE)	0.9278 (0.4442, 1.9376) 0.8418	0.8308	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.1643
Positive	331	167 (50.5)	164 (49.5)	7.5 (4.8, 12.0)	155	53 (34.2)	102 (65.8)	NE (7.1, NE)	1.3316 (0.9753, 1.8183) 0.0715	0.0720	
Negative	40	21 (52.5)	19 (47.5)	6.2 (0.3, NE)	17	10 (58.8)	7 (41.2)	1.4 (0.3, NE)	0.8143 (0.3746, 1.7704) 0.6042	0.5821	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.4023
HER2 IHC 1+	214	68 (31.8)	146 (68.2)	NE (NE, NE)	100	17 (17.0)	83 (83.0)	NE (NE, NE)	1.8200 (1.0672, 3.1037) 0.0279	0.0264	
HER2 IHC 2+/ISH Negative	157	50 (31.8)	107 (68.2)	NE (NE, NE)	72	16 (22.2)	56 (77.8)	NE (NE, NE)	1.3138 (0.7456, 2.3149) 0.3451	0.3465	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.6990
1	220	70 (31.8)	150 (68.2)	NE (NE, NE)	94	17 (18.1)	77 (81.9)	NE (NE, NE)	1.7038 (1.0014, 2.8987) 0.0494	0.0474	
>=2	150	47 (31.3)	103 (68.7)	NE (NE, NE)	78	16 (20.5)	62 (79.5)	NE (NE, NE)	1.4348 (0.8100, 2.5417) 0.2159	0.2163	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.7356
Yes	233	66 (28.3)	167 (71.7)	NE (NE, NE)	112	16 (14.3)	96 (85.7)	NE (NE, NE)	1.7998 (1.0386, 3.1190) 0.0362	0.0333	
No	98	39 (39.8)	59 (60.2)	NE (6.5, NE)	43	11 (25.6)	32 (74.4)	NE (NE, NE)	1.5891 (0.8123, 3.1090) 0.1761	0.1776	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2866
<65	289	92 (31.8)	197 (68.2)	NE (NE, NE)	126	21 (16.7)	105 (83.3)	NE (NE, NE)	1.8029 (1.1189, 2.9050) 0.0155	0.0147	
>=65	82	26 (31.7)	56 (68.3)	NE (NE, NE)	46	12 (26.1)	34 (73.9)	NE (NE, NE)	1.1681 (0.5889, 2.3170) 0.6566	0.6506	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5825
<75	357	114 (31.9)	243 (68.1)	NE (NE, NE)	163	32 (19.6)	131 (80.4)	NE (NE, NE)	1.5252 (1.0281, 2.2628) 0.0359	0.0356	
>=75	14	4 (28.6)	10 (71.4)	NE (0.9, NE)	9	1 (11.1)	8 (88.9)	NE (1.0, NE)	2.9932 (0.3337, 26.8529) 0.3274	0.3036	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.4726
White	175	39 (22.3)	136 (77.7)	NE (NE, NE)	85	13 (15.3)	72 (84.7)	NE (NE, NE)	1.2510 (0.6643, 2.3560) 0.4880	0.4868	
Non-White	196	79 (40.3)	117 (59.7)	NE (7.2, NE)	86	20 (23.3)	66 (76.7)	NE (NE, NE)	1.7631 (1.0773, 2.8855) 0.0241	0.0234	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.7473
Asia	147	65 (44.2)	82 (55.8)	NE (4.3, NE)	63	19 (30.2)	44 (69.8)	NE (6.5, NE)	1.4351 (0.8581, 2.4000) 0.1686	0.1735	
North America	58	9 (15.5)	49 (84.5)	NE (NE, NE)	28	3 (10.7)	25 (89.3)	NE (NE, NE)	1.1821 (0.3122, 4.4763) 0.8055	0.8063	
Europe + Israel	166	44 (26.5)	122 (73.5)	NE (NE, NE)	81	11 (13.6)	70 (86.4)	NE (NE, NE)	1.8625 (0.9589, 3.6174) 0.0663	0.0630	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.5082
0	199	55 (27.6)	144 (72.4)	NE (NE, NE)	95	17 (17.9)	78 (82.1)	NE (NE, NE)	1.3843 (0.8009, 2.3926) 0.2441	0.2421	
1	172	63 (36.6)	109 (63.4)	NE (14.5, NE)	77	16 (20.8)	61 (79.2)	NE (6.5, NE)	1.8017 (1.0381, 3.1267) 0.0363	0.0349	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.0116
0	60	19 (31.7)	41 (68.3)	NE (NE, NE)	31	12 (38.7)	19 (61.3)	NE (1.4, NE)	0.7955 (0.3834, 1.6505) 0.5389	0.5180	
1	107	33 (30.8)	74 (69.2)	NE (NE, NE)	48	10 (20.8)	38 (79.2)	NE (NE, NE)	1.4901 (0.7338, 3.0261) 0.2698	0.2663	
2	114	34 (29.8)	80 (70.2)	NE (NE, NE)	50	2 (4.0)	48 (96.0)	NE (6.5, NE)	6.8328 (1.6361, 28.5363) 0.0084	0.0023	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	32 (35.6)	58 (64.4)	NE (14.5, NE)	43	9 (20.9)	34 (79.1)	NE (NE, NE)	1.5112 (0.7164, 3.1879) 0.2783	0.2750	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.1801
PD	173	48 (27.7)	125 (72.3)	NE (NE, NE)	77	13 (16.9)	64 (83.1)	NE (NE, NE)	1.5114 (0.8163, 2.7982)	0.1872	
PR	48	20 (41.7)	28 (58.3)	14.5 (4.1, NE)	21	2 (9.5)	19 (90.5)	NE (NE, NE)	4.0187 (0.9329, 17.3111)	0.0437	
SD	82	25 (30.5)	57 (69.5)	NE (NE, NE)	54	14 (25.9)	40 (74.1)	NE (NE, NE)	1.1524 (0.5972, 2.2238)	0.6791	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.8229
Yes	37	16 (43.2)	21 (56.8)	13.2 (1.5, NE)	13	3 (23.1)	10 (76.9)	NE (0.8, NE)	1.6962 (0.4886, 5.8886) 0.4054	0.3974	
No	334	102 (30.5)	232 (69.5)	NE (NE, NE)	159	30 (18.9)	129 (81.1)	NE (NE, NE)	1.5347 (1.0194, 2.3105) 0.0402	0.0395	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.6623
Yes	24	12 (50.0)	12 (50.0)	4.9 (0.1, NE)	7	3 (42.9)	4 (57.1)	NE (0.1, NE)	1.2076 (0.3402, 4.2864) 0.7704	0.7670	
No	347	106 (30.5)	241 (69.5)	NE (NE, NE)	165	30 (18.2)	135 (81.8)	NE (NE, NE)	1.5767 (1.0489, 2.3701) 0.0286	0.0278	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.7409
Normal Function	201	61 (30.3)	140 (69.7)	NE (NE, NE)	80	14 (17.5)	66 (82.5)	NE (NE, NE)	1.6469 (0.9184, 2.9532) 0.0941	0.0926	
Mild Impairment	123	44 (35.8)	79 (64.2)	NE (14.5, NE)	65	14 (21.5)	51 (78.5)	NE (NE, NE)	1.5866 (0.8662, 2.9062) 0.1350	0.1346	
Moderate Impairment	41	10 (24.4)	31 (75.6)	NE (NE, NE)	23	5 (21.7)	18 (78.3)	NE (NE, NE)	1.0094 (0.3444, 2.9587) 0.9864	0.9806	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.0529
Normal Function	170	55 (32.4)	115 (67.6)	NE (NE, NE)	88	23 (26.1)	65 (73.9)	NE (NE, NE)	1.1021 (0.6743, 1.8012) 0.6982	0.7117	
Mild Impairment	194	61 (31.4)	133 (68.6)	NE (NE, NE)	82	10 (12.2)	72 (87.8)	NE (NE, NE)	2.5761 (1.3180, 5.0351) 0.0056	0.0041	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.9684
Yes	331	99 (29.9)	232 (70.1)	NE (NE, NE)	146	26 (17.8)	120 (82.2)	NE (NE, NE)	1.6136 (1.0457, 2.4898) 0.0306	0.0296	
No	40	19 (47.5)	21 (52.5)	6.5 (2.3, NE)	26	7 (26.9)	19 (73.1)	NE (2.2, NE)	1.5454 (0.6416, 3.7220) 0.3318	0.3343	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.2358
Positive	329	104 (31.6)	225 (68.4)	NE (NE, NE)	152	26 (17.1)	126 (82.9)	NE (NE, NE)	1.7438 (1.1324, 2.6854)	0.0107	
Negative	42	14 (33.3)	28 (66.7)	NE (6.2, NE)	20	7 (35.0)	13 (65.0)	NE (1.0, NE)	0.9616 (0.3857, 2.3970)	0.9212	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Metabolism and nutrition disorders; PT: Decreased appetite

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.2436
Positive	331	105 (31.7)	226 (68.3)	NE (NE, NE)	155	27 (17.4)	128 (82.6)	NE (NE, NE)	1.7184 (1.1236, 2.6281) 0.0125	0.0117	
Negative	40	13 (32.5)	27 (67.5)	NE (6.2, NE)	17	6 (35.3)	11 (64.7)	NE (1.0, NE)	0.9298 (0.3505, 2.4664) 0.8838	0.8617	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.4724
HER2 IHC 1+	214	24 (11.2)	190 (88.8)	NE (NE, NE)	100	6 (6.0)	94 (94.0)	NE (NE, NE)	1.3142 (0.5297, 3.2606) 0.5556	0.5546	
HER2 IHC 2+/ISH Negative	157	15 (9.6)	142 (90.4)	NE (NE, NE)	72	6 (8.3)	66 (91.7)	NE (NE, NE)	0.8158 (0.3122, 2.1317) 0.6779	0.6762	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.1528
1	220	22 (10.0)	198 (90.0)	NE (NE, NE)	94	9 (9.6)	85 (90.4)	NE (NE, NE)	0.7072 (0.3211, 1.5575) 0.3897	0.3873	
>=2	150	17 (11.3)	133 (88.7)	NE (NE, NE)	78	3 (3.8)	75 (96.2)	NE (NE, NE)	2.2864 (0.6625, 7.8905) 0.1907	0.1788	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.1796
Yes	233	18 (7.7)	215 (92.3)	NE (NE, NE)	112	8 (7.1)	104 (92.9)	NE (NE, NE)	0.7388 (0.3157, 1.7288) 0.4852	0.4829	
No	98	17 (17.3)	81 (82.7)	NE (NE, NE)	43	3 (7.0)	40 (93.0)	NE (NE, NE)	1.9611 (0.5712, 6.7332) 0.2846	0.2757	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5137
<65	289	30 (10.4)	259 (89.6)	NE (NE, NE)	126	7 (5.6)	119 (94.4)	NE (NE, NE)	1.3180 (0.5718, 3.0382) 0.5170	0.5155	
>=65	82	9 (11.0)	73 (89.0)	NE (NE, NE)	46	5 (10.9)	41 (89.1)	NE (NE, NE)	0.7912 (0.2624, 2.3858) 0.6775	0.6769	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2471
<75	357	38 (10.6)	319 (89.4)	NE (NE, NE)	163	10 (6.1)	153 (93.9)	NE (NE, NE)	1.2060 (0.5946, 2.4457) 0.6037	0.6035	
>=75	14	1 (7.1)	13 (92.9)	NE (NE, NE)	9	2 (22.2)	7 (77.8)	NE (0.6, NE)	0.3215 (0.0290, 3.5599) 0.3550	0.3296	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.8806
White	175	21 (12.0)	154 (88.0)	NE (NE, NE)	85	7 (8.2)	78 (91.8)	NE (NE, NE)	1.1074 (0.4658, 2.6330) 0.8174	0.8190	
Non-White	196	18 (9.2)	178 (90.8)	NE (NE, NE)	86	5 (5.8)	81 (94.2)	NE (NE, NE)	1.0316 (0.3764, 2.8268) 0.9518	0.9513	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.9116
Asia	147	15 (10.2)	132 (89.8)	NE (NE, NE)	63	5 (7.9)	58 (92.1)	NE (NE, NE)	0.7963 (0.2840, 2.2326) 0.6650	0.6647	
North America	58	11 (19.0)	47 (81.0)	NE (NE, NE)	28	3 (10.7)	25 (89.3)	NE (NE, NE)	1.5561 (0.4296, 5.6362) 0.5007	0.4990	
Europe + Israel	166	13 (7.8)	153 (92.2)	NE (NE, NE)	81	4 (4.9)	77 (95.1)	NE (NE, NE)	1.1182 (0.3596, 3.4778) 0.8469	0.8480	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.9897
0	199	17 (8.5)	182 (91.5)	NE (NE, NE)	95	5 (5.3)	90 (94.7)	NE (NE, NE)	1.0351 (0.3758, 2.8514) 0.9468	0.9466	
1	172	22 (12.8)	150 (87.2)	NE (NE, NE)	77	7 (9.1)	70 (90.9)	NE (NE, NE)	1.1277 (0.4761, 2.6710) 0.7848	0.7848	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.7460
0	60	8 (13.3)	52 (86.7)	NE (NE, NE)	31	2 (6.5)	29 (93.5)	NE (5.4, NE)	1.4618 (0.3008, 7.1034) 0.6379	0.6358	
1	107	14 (13.1)	93 (86.9)	NE (NE, NE)	48	5 (10.4)	43 (89.6)	NE (NE, NE)	1.0444 (0.3742, 2.9151) 0.9339	0.9330	
2	114	11 (9.6)	103 (90.4)	NE (NE, NE)	50	2 (4.0)	48 (96.0)	NE (NE, NE)	1.6308 (0.3541, 7.5096) 0.5302	0.5272	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	6 (6.7)	84 (93.3)	NE (NE, NE)	43	3 (7.0)	40 (93.0)	NE (NE, NE)	0.5711 (0.1348, 2.4197) 0.4470	0.4417	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.1934
PD	173	18 (10.4)	155 (89.6)	NE (NE, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	2.9095 (0.6692, 12.6508) 0.1544	0.1358	
PR	48	4 (8.3)	44 (91.7)	NE (NE, NE)	21	2 (9.5)	19 (90.5)	NE (NE, NE)	0.5408 (0.0932, 3.1373) 0.4932	0.4878	
SD	82	7 (8.5)	75 (91.5)	NE (NE, NE)	54	5 (9.3)	49 (90.7)	NE (NE, NE)	0.6983 (0.2178, 2.2387) 0.5458	0.5438	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.3673
Yes	37	2 (5.4)	35 (94.6)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9975	0.4852	
No	334	37 (11.1)	297 (88.9)	NE (NE, NE)	159	12 (7.5)	147 (92.5)	NE (NE, NE)	1.0454 (0.5394, 2.0260) 0.8954	0.8952	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.3533
Yes	24	2 (8.3)	22 (91.7)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9973	0.4511	
No	347	37 (10.7)	310 (89.3)	NE (NE, NE)	165	12 (7.3)	153 (92.7)	NE (NE, NE)	1.0294 (0.5309, 1.9961) 0.9317	0.9321	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.5515
Normal Function	201	25 (12.4)	176 (87.6)	NE (NE, NE)	80	6 (7.5)	74 (92.5)	NE (NE, NE)	1.1957 (0.4841, 2.9534) 0.6984	0.6983	
Mild Impairment	123	7 (5.7)	116 (94.3)	NE (NE, NE)	65	4 (6.2)	61 (93.8)	NE (NE, NE)	0.5595 (0.1576, 1.9867) 0.3691	0.3632	
Moderate Impairment	41	7 (17.1)	34 (82.9)	NE (NE, NE)	23	2 (8.7)	21 (91.3)	NE (NE, NE)	1.8420 (0.3822, 8.8773) 0.4465	0.4394	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.2430
Normal Function	170	18 (10.6)	152 (89.4)	NE (NE, NE)	88	4 (4.5)	84 (95.5)	NE (NE, NE)	1.5349 (0.5106, 4.6141) 0.4454	0.4414	
Mild Impairment	194	21 (10.8)	173 (89.2)	NE (NE, NE)	82	8 (9.8)	74 (90.2)	NE (NE, NE)	0.8113 (0.3556, 1.8510) 0.6193	0.6181	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.8888
Yes	331	34 (10.3)	297 (89.7)	NE (NE, NE)	146	10 (6.8)	136 (93.2)	NE (NE, NE)	1.1292 (0.5536, 2.3031) 0.7383	0.7387	
No	40	5 (12.5)	35 (87.5)	NE (NE, NE)	26	2 (7.7)	24 (92.3)	NE (5.4, NE)	0.7015 (0.1208, 4.0725) 0.6928	0.6916	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.8154
Positive	329	35 (10.6)	294 (89.4)	NE (NE, NE)	152	11 (7.2)	141 (92.8)	NE (NE, NE)	1.0425 (0.5249, 2.0708)	0.9052	
Negative	42	4 (9.5)	38 (90.5)	NE (11.7, NE)	20	1 (5.0)	19 (95.0)	NE (NE, NE)	1.4804 (0.1540, 14.2331)	0.7323	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.8378
Positive	331	36 (10.9)	295 (89.1)	NE (NE, NE)	155	11 (7.1)	144 (92.9)	NE (NE, NE)	1.1021 (0.5561, 2.1841)	0.7812	
Negative	40	3 (7.5)	37 (92.5)	NE (11.7, NE)	17	1 (5.9)	16 (94.1)	NE (NE, NE)	0.8353 (0.0757, 9.2223)	0.8831	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypoalbuminaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.4495
HER2 IHC 1+	214	17 (7.9)	197 (92.1)	NE (23.7, NE)	100	3 (3.0)	97 (97.0)	NE (NE, NE)	1.5178 (0.4329, 5.3220) 0.5145	0.5110	
HER2 IHC 2+/ISH Negative	157	15 (9.6)	142 (90.4)	NE (NE, NE)	72	5 (6.9)	67 (93.1)	NE (10.1, NE)	1.0690 (0.3832, 2.9826) 0.8986	0.8971	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Metabolism and nutrition disorders; PT: Hypoalbuminaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.1016
1	220	15 (6.8)	205 (93.2)	NE (NE, NE)	94	6 (6.4)	88 (93.6)	NE (NE, NE)	0.7564 (0.2891, 1.9786) 0.5693	0.5683	
>=2	150	17 (11.3)	133 (88.7)	NE (19.6, NE)	78	2 (2.6)	76 (97.4)	NE (NE, NE)	2.8656 (0.6469, 12.6938) 0.1656	0.1469	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypoalbuminaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.7683
Yes	233	18 (7.7)	215 (92.3)	NE (23.7, NE)	112	4 (3.6)	108 (96.4)	NE (10.1, NE)	1.2474 (0.4075, 3.8181) 0.6985	0.6992	
No	98	11 (11.2)	87 (88.8)	NE (NE, NE)	43	3 (7.0)	40 (93.0)	NE (NE, NE)	1.3143 (0.3647, 4.7361) 0.6760	0.6735	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Metabolism and nutrition disorders; PT: Hypoalbuminaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8109
<65	289	25 (8.7)	264 (91.3)	NE (NE, NE)	126	6 (4.8)	120 (95.2)	NE (NE, NE)	1.1321 (0.4545, 2.8197) 0.7899	0.7884	
>=65	82	7 (8.5)	75 (91.5)	NE (NE, NE)	46	2 (4.3)	44 (95.7)	NE (NE, NE)	1.6051 (0.3285, 7.8431) 0.5588	0.5558	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypoalbuminaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3642
<75	357	31 (8.7)	326 (91.3)	NE (NE, NE)	163	8 (4.9)	155 (95.1)	NE (NE, NE)	1.1490 (0.5188, 2.5445) 0.7321	0.7309	
>=75	14	1 (7.1)	13 (92.9)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9985	0.4227	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.3610
White	175	13 (7.4)	162 (92.6)	NE (23.7, NE)	85	2 (2.4)	83 (97.6)	NE (10.1, NE)	2.0237 (0.4415, 9.2773) 0.3642	0.3549	
Non-White	196	19 (9.7)	177 (90.3)	NE (NE, NE)	86	6 (7.0)	80 (93.0)	NE (NE, NE)	0.9829 (0.3880, 2.4903) 0.9711	0.9724	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Metabolism and nutrition disorders; PT: Hypoalbuminaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.2092
Asia	147	17 (11.6)	130 (88.4)	NE (NE, NE)	63	3 (4.8)	60 (95.2)	NE (NE, NE)	1.6402 (0.4744, 5.6709) 0.4343	0.4294	
North America	58	6 (10.3)	52 (89.7)	23.7 (19.6, 23.7)	28	4 (14.3)	24 (85.7)	10.1 (10.1, NE)	0.3284 (0.0787, 1.3709) 0.1267	0.1096	
Europe + Israel	166	9 (5.4)	157 (94.6)	NE (NE, NE)	81	1 (1.2)	80 (98.8)	NE (NE, NE)	3.6750 (0.4617, 29.2533) 0.2188	0.1879	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypoalbuminaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.2846
0	199	15 (7.5)	184 (92.5)	NE (NE, NE)	95	2 (2.1)	93 (97.9)	NE (NE, NE)	2.0701 (0.4629, 9.2580) 0.3411	0.3306	
1	172	17 (9.9)	155 (90.1)	NE (23.7, NE)	77	6 (7.8)	71 (92.2)	NE (10.1, NE)	0.9513 (0.3676, 2.4614) 0.9179	0.9192	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypoalbuminaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.3089
0	60	5 (8.3)	55 (91.7)	NE (NE, NE)	31	1 (3.2)	30 (96.8)	NE (NE, NE)	1.9870 (0.2283, 17.2929) 0.5340	0.5262	
1	107	14 (13.1)	93 (86.9)	NE (19.6, NE)	48	2 (4.2)	46 (95.8)	NE (NE, NE)	2.6117 (0.5881, 11.5975) 0.2069	0.1895	
2	114	9 (7.9)	105 (92.1)	NE (23.7, NE)	50	2 (4.0)	48 (96.0)	NE (NE, NE)	1.0201 (0.2068, 5.0327) 0.9805	0.9804	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypoalbuminaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	4 (4.4)	86 (95.6)	NE (NE, NE)	43	3 (7.0)	40 (93.0)	NE (10.1, NE)	0.3447 (0.0696, 1.7078) 0.1921	0.1757	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypoalbuminaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.5837
PD	173	12 (6.9)	161 (93.1)	NE (NE, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	1.2502 (0.3462, 4.5146)	0.7323	
PR	48	2 (4.2)	46 (95.8)	NE (NE, NE)	21	1 (4.8)	20 (95.2)	NE (NE, NE)	0.5612 (0.0467, 6.7405)	0.6447	
SD	82	6 (7.3)	76 (92.7)	NE (23.7, NE)	54	1 (1.9)	53 (98.1)	NE (NE, NE)	2.6681 (0.3098, 22.9810)	0.3529	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Hypoalbuminaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.3033
Yes	37	3 (8.1)	34 (91.9)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9966	0.3422	
No	334	29 (8.7)	305 (91.3)	NE (NE, NE)	159	8 (5.0)	151 (95.0)	NE (NE, NE)	1.1286 (0.5066, 2.5145) 0.7672	0.7666	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypoalbuminaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.2928
Yes	24	3 (12.5)	21 (87.5)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9967	0.3578	
No	347	29 (8.4)	318 (91.6)	NE (NE, NE)	165	8 (4.8)	157 (95.2)	NE (NE, NE)	1.1115 (0.4985, 2.4783) 0.7961	0.7956	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypoalbuminaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.5356
Normal Function	201	16 (8.0)	185 (92.0)	NE (23.7, NE)	80	5 (6.3)	75 (93.8)	NE (10.1, NE)	0.7356 (0.2590, 2.0892) 0.5643	0.5639	
Mild Impairment	123	12 (9.8)	111 (90.2)	NE (NE, NE)	65	2 (3.1)	63 (96.9)	NE (NE, NE)	2.2974 (0.5057, 10.4360) 0.2814	0.2678	
Moderate Impairment	41	4 (9.8)	37 (90.2)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	2.0355 (0.2266, 18.2817) 0.5257	0.5189	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Hypoalbuminaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.7425
Normal Function	170	12 (7.1)	158 (92.9)	NE (23.7, NE)	88	3 (3.4)	85 (96.6)	NE (NE, NE)	1.3728 (0.3780, 4.9854) 0.6301	0.6283	
Mild Impairment	194	19 (9.8)	175 (90.2)	NE (NE, NE)	82	5 (6.1)	77 (93.9)	NE (10.1, NE)	1.0401 (0.3793, 2.8522) 0.9391	0.9364	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Hypoalbuminaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.8736
Yes	331	28 (8.5)	303 (91.5)	NE (NE, NE)	146	7 (4.8)	139 (95.2)	NE (NE, NE)	1.2066 (0.5183, 2.8089) 0.6631	0.6621	
No	40	4 (10.0)	36 (90.0)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	1.6128 (0.1756, 14.8092) 0.6727	0.6699	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypoalbuminaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.7786
Positive	329	29 (8.8)	300 (91.2)	NE (NE, NE)	152	7 (4.6)	145 (95.4)	NE (NE, NE)	1.2719 (0.5483, 2.9507)	0.5738	
Negative	42	3 (7.1)	39 (92.9)	NE (NE, NE)	20	1 (5.0)	19 (95.0)	NE (NE, NE)	1.1394 (0.1142, 11.3653)	0.9115	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypoalbuminaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.6789
Positive	331	29 (8.8)	302 (91.2)	NE (NE, NE)	155	7 (4.5)	148 (95.5)	NE (NE, NE)	1.2923 (0.5570, 2.9982)	0.5488	
Negative	40	3 (7.5)	37 (92.5)	NE (NE, NE)	17	1 (5.9)	16 (94.1)	NE (NE, NE)	1.0318 (0.1040, 10.2325)	0.9785	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Metabolism and nutrition disorders; PT: Hypocalcaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.1748
HER2 IHC 1+	214	10 (4.7)	204 (95.3)	NE (NE, NE)	100	1 (1.0)	99 (99.0)	NE (NE, NE)	3.7085 (0.4681, 29.3814) 0.2146	0.1835	
HER2 IHC 2+/ISH Negative	157	9 (5.7)	148 (94.3)	NE (NE, NE)	72	4 (5.6)	68 (94.4)	NE (NE, NE)	0.7154 (0.2136, 2.3962) 0.5871	0.5855	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Metabolism and nutrition disorders; PT: Hypocalcaemia

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.4878
1	220	9 (4.1)	211 (95.9)	NE (NE, NE)	94	3 (3.2)	91 (96.8)	NE (NE, NE)	1.1267 (0.3029, 4.1910) 0.8587	0.8583	
>=2	150	10 (6.7)	140 (93.3)	NE (NE, NE)	78	2 (2.6)	76 (97.4)	NE (NE, NE)	1.6242 (0.3423, 7.7073) 0.5416	0.5354	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.3065
Yes	233	14 (6.0)	219 (94.0)	NE (NE, NE)	112	3 (2.7)	109 (97.3)	NE (NE, NE)	1.5232 (0.4248, 5.4610) 0.5183	0.5147	
No	98	3 (3.1)	95 (96.9)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9967	0.3365	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2251
<65	289	11 (3.8)	278 (96.2)	NE (NE, NE)	126	1 (0.8)	125 (99.2)	NE (NE, NE)	3.5326 (0.4478, 27.8708) 0.2311	0.2015	
>=65	82	8 (9.8)	74 (90.2)	NE (NE, NE)	46	4 (8.7)	42 (91.3)	NE (NE, NE)	0.9140 (0.2714, 3.0774) 0.8845	0.8872	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1633
<75	357	18 (5.0)	339 (95.0)	NE (NE, NE)	163	3 (1.8)	160 (98.2)	NE (NE, NE)	1.9311 (0.5580, 6.6834) 0.2988	0.2904	
>=75	14	1 (7.1)	13 (92.9)	NE (NE, NE)	9	2 (22.2)	7 (77.8)	NE (1.4, NE)	0.3509 (0.0318, 3.8726) 0.3927	0.3829	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.1073
White	175	14 (8.0)	161 (92.0)	NE (NE, NE)	85	5 (5.9)	80 (94.1)	NE (NE, NE)	0.9216 (0.3225, 2.6333) 0.8789	0.8800	
Non-White	196	5 (2.6)	191 (97.4)	NE (NE, NE)	86	0	86 (100)	NE (NE, NE)	NE (NE, NE) 0.9954	0.1688	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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[c] Two-sided p-value from unstratified log-rank test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.5400
Asia	147	2 (1.4)	145 (98.6)	NE (NE, NE)	63	0	63 (100)	NE (NE, NE)	NE (NE, NE) 0.9974	0.4652	
North America	58	6 (10.3)	52 (89.7)	NE (NE, NE)	28	1 (3.6)	27 (96.4)	NE (NE, NE)	1.7957 (0.2004, 16.0917) 0.6008	0.5956	
Europe + Israel	166	11 (6.6)	155 (93.4)	NE (NE, NE)	81	4 (4.9)	77 (95.1)	NE (NE, NE)	1.0522 (0.3284, 3.3708) 0.9317	0.9300	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.7977
0	199	5 (2.5)	194 (97.5)	NE (NE, NE)	95	1 (1.1)	94 (98.9)	NE (NE, NE)	1.3693 (0.1518, 12.3527) 0.7794	0.7785	
1	172	14 (8.1)	158 (91.9)	NE (NE, NE)	77	4 (5.2)	73 (94.8)	NE (NE, NE)	1.3050 (0.4233, 4.0237) 0.6431	0.6412	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.4910
0	60	3 (5.0)	57 (95.0)	NE (NE, NE)	31	2 (6.5)	29 (93.5)	NE (NE, NE)	0.5387 (0.0821, 3.5343) 0.5193	0.5182	
1	107	5 (4.7)	102 (95.3)	NE (NE, NE)	48	2 (4.2)	46 (95.8)	NE (NE, NE)	0.9858 (0.1897, 5.1245) 0.9865	0.9865	
2	114	9 (7.9)	105 (92.1)	NE (NE, NE)	50	1 (2.0)	49 (98.0)	NE (NE, NE)	2.4938 (0.3022, 20.5790) 0.3961	0.3806	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypocalcaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	2 (2.2)	88 (97.8)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9969	0.3559	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypocalcaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.7508
PD	173	8 (4.6)	165 (95.4)	NE (NE, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	0.9883 (0.2576, 3.7921)	0.9881	
PR	48	1 (2.1)	47 (97.9)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	0.9863 (NE, NE)	0.7576	
SD	82	5 (6.1)	77 (93.9)	NE (NE, NE)	54	2 (3.7)	52 (96.3)	NE (NE, NE)	1.0280 (0.1897, 5.5706)	0.9744	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Hypocalcaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.2569
Yes	37	1 (2.7)	36 (97.3)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	0.3376 (0.0211, 5.3999)	0.4202	
No	334	18 (5.4)	316 (94.6)	NE (NE, NE)	159	4 (2.5)	155 (97.5)	NE (NE, NE)	1.5445 (0.5131, 4.6486)	0.4345	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypocalcaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.5438
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9981	0.5892	
No	347	18 (5.2)	329 (94.8)	NE (NE, NE)	165	5 (3.0)	160 (97.0)	NE (NE, NE)	1.2332 (0.4487, 3.3890) 0.6845	0.6830	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypocalcaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.1694
Normal Function	201	7 (3.5)	194 (96.5)	NE (NE, NE)	80	0	80 (100)	NE (NE, NE)	NE (NE, NE) 0.9930	0.1993	
Mild Impairment	123	6 (4.9)	117 (95.1)	NE (NE, NE)	65	3 (4.6)	62 (95.4)	NE (NE, NE)	0.7241 (0.1735, 3.0210) 0.6578	0.6565	
Moderate Impairment	41	4 (9.8)	37 (90.2)	NE (NE, NE)	23	2 (8.7)	21 (91.3)	NE (NE, NE)	1.0325 (0.1888, 5.6466) 0.9705	0.9704	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypocalcaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.8657
Normal Function	170	5 (2.9)	165 (97.1)	NE (NE, NE)	88	2 (2.3)	86 (97.7)	NE (NE, NE)	0.9563 (0.1796, 5.0911) 0.9582	0.9604	
Mild Impairment	194	11 (5.7)	183 (94.3)	NE (NE, NE)	82	3 (3.7)	79 (96.3)	NE (NE, NE)	1.0199 (0.2743, 3.7916) 0.9766	0.9762	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Hypocalcaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.9526
Yes	331	16 (4.8)	315 (95.2)	NE (NE, NE)	146	4 (2.7)	142 (97.3)	NE (NE, NE)	1.3173 (0.4329, 4.0086) 0.6274	0.6258	
No	40	3 (7.5)	37 (92.5)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	1.3826 (0.1288, 14.8386) 0.7890	0.7882	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypocalcaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.2860
Positive	329	16 (4.9)	313 (95.1)	NE (NE, NE)	152	3 (2.0)	149 (98.0)	NE (NE, NE)	1.7085 (0.4885, 5.9752)	0.3962	
Negative	42	3 (7.1)	39 (92.9)	NE (NE, NE)	20	2 (10.0)	18 (90.0)	NE (NE, NE)	0.7543 (0.1260, 4.5150)	0.7645	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypocalcaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.1232
Positive	331	17 (5.1)	314 (94.9)	NE (NE, NE)	155	3 (1.9)	152 (98.1)	NE (NE, NE)	1.8888 (0.5440, 6.5584)	0.3087	
Negative	40	2 (5.0)	38 (95.0)	NE (NE, NE)	17	2 (11.8)	15 (88.2)	NE (NE, NE)	0.4437 (0.0625, 3.1504)	0.4107	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypercalcaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.1361
HER2 IHC 1+	214	7 (3.3)	207 (96.7)	NE (NE, NE)	100	0	100 (100)	NE (NE, NE)	NE (NE, NE) 0.9951	0.1576	
HER2 IHC 2+/ISH Negative	157	5 (3.2)	152 (96.8)	NE (NE, NE)	72	1 (1.4)	71 (98.6)	NE (NE, NE)	1.6103 (0.1815, 14.2899) 0.6689	0.6667	
HER2 IHC 1+	214	6 (2.8)	208 (97.2)	NE (NE, NE)	100	1 (1.0)	99 (99.0)	NE (NE, NE)	2.5463 (0.3055, 21.2270) 0.3877	0.3711	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hyponatraemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.1361
HER2 IHC 2+/ISH Negative	157	6 (3.8)	151 (96.2)	NE (NE, NE)	72	4 (5.6)	68 (94.4)	NE (NE, NE)	0.5405 (0.1497, 1.9520) 0.3477	0.3411	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypercalcaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.1162
1	220	5 (2.3)	215 (97.7)	NE (NE, NE)	94	1 (1.1)	93 (98.9)	NE (NE, NE)	1.5745 (0.1797, 13.7925) 0.6818	0.6793	
>=2	150	7 (4.7)	143 (95.3)	NE (NE, NE)	78	0	78 (100)	NE (NE, NE)	NE (NE, NE) 0.9952	0.1547	
1	220	3 (1.4)	217 (98.6)	NE (NE, NE)	94	2 (2.1)	92 (97.9)	NE (NE, NE)	0.4954 (0.0824, 2.9774) 0.4427	0.4356	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hyponatraemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											NE
>=2	150	9 (6.0)	141 (94.0)	NE (NE, NE)	78	3 (3.8)	75 (96.2)	NE (NE, NE)	1.3860 (0.3709, 5.1788) 0.6274	0.6256	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypercalcaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.2518
Yes	233	6 (2.6)	227 (97.4)	NE (NE, NE)	112	1 (0.9)	111 (99.1)	NE (NE, NE)	2.0426 (0.2367, 17.6241) 0.5160	0.5077	
No	98	6 (6.1)	92 (93.9)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9954	0.1926	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Metabolism and nutrition disorders; PT: Hyponatraemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.6925
Yes	233	7 (3.0)	226 (97.0)	NE (NE, NE)	112	4 (3.6)	108 (96.4)	NE (NE, NE)	0.6108 (0.1750, 2.1314) 0.4394	0.4370	
No	98	3 (3.1)	95 (96.9)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	1.2988 (0.1351, 12.4864) 0.8209	0.8217	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Metabolism and nutrition disorders; PT: Hypercalcaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4910
<65	289	10 (3.5)	279 (96.5)	NE (NE, NE)	126	1 (0.8)	125 (99.2)	NE (NE, NE)	2.7822 (0.3484, 22.2160) 0.3344	0.3141	
>=65	82	2 (2.4)	80 (97.6)	NE (NE, NE)	46	0	46 (100)	NE (NE, NE)	NE (NE, NE) 0.9974	0.4300	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hyponatraemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7722
<65	289	9 (3.1)	280 (96.9)	NE (NE, NE)	126	3 (2.4)	123 (97.6)	NE (NE, NE)	1.2093 (0.3263, 4.4813) 0.7761	0.7762	
>=65	82	3 (3.7)	79 (96.3)	NE (NE, NE)	46	2 (4.3)	44 (95.7)	NE (NE, NE)	0.6406 (0.1051, 3.9042) 0.6292	0.6320	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Metabolism and nutrition disorders; PT: Hypercalcaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9998
<75	357	12 (3.4)	345 (96.6)	NE (NE, NE)	163	1 (0.6)	162 (99.4)	NE (NE, NE)	3.4866 (0.4438, 27.3890)	0.2064	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE)	NE	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Metabolism and nutrition disorders; PT: Hyponatraemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3057
<75	357	11 (3.1)	346 (96.9)	NE (NE, NE)	163	5 (3.1)	158 (96.9)	NE (NE, NE)	0.8422 (0.2897, 2.4485) 0.7525	0.7520	
>=75	14	1 (7.1)	13 (92.9)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9985	0.4142	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Metabolism and nutrition disorders; PT: Hypercalcaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.2584
White	175	6 (3.4)	169 (96.6)	NE (NE, NE)	85	1 (1.2)	84 (98.8)	NE (NE, NE)	1.5996 (0.1865, 13.7163) 0.6683	0.6656	
Non-White	196	6 (3.1)	190 (96.9)	NE (NE, NE)	86	0	86 (100)	NE (NE, NE)	NE (NE, NE) 0.9953	0.1639	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hyponatraemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.6186
White	175	8 (4.6)	167 (95.4)	NE (NE, NE)	85	4 (4.7)	81 (95.3)	NE (NE, NE)	0.7372 (0.2185, 2.4880) 0.6233	0.6247	
Non-White	196	4 (2.0)	192 (98.0)	NE (NE, NE)	86	1 (1.2)	85 (98.8)	NE (NE, NE)	1.7467 (0.1952, 15.6272) 0.6179	0.6146	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypercalcaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.4739
Asia	147	5 (3.4)	142 (96.6)	NE (NE, NE)	63	0	63 (100)	NE (NE, NE)	NE (NE, NE) 0.9958	0.2262	
North America	58	2 (3.4)	56 (96.6)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9978	0.5290	
Europe + Israel	166	5 (3.0)	161 (97.0)	NE (NE, NE)	81	1 (1.2)	80 (98.8)	NE (NE, NE)	1.7092 (0.1954, 14.9528) 0.6281	0.6242	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Metabolism and nutrition disorders; PT: Hyponatraemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.9059
Asia	147	4 (2.7)	143 (97.3)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (NE, NE)	1.7001 (0.1900, 15.2105) 0.6350	0.6328	
North America	58	4 (6.9)	54 (93.1)	NE (NE, NE)	28	2 (7.1)	26 (92.9)	NE (NE, NE)	0.8125 (0.1481, 4.4566) 0.8110	0.8118	
Europe + Israel	166	4 (2.4)	162 (97.6)	NE (NE, NE)	81	2 (2.5)	79 (97.5)	NE (NE, NE)	0.7202 (0.1279, 4.0538) 0.7097	0.7088	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypercalcaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.2015
0	199	7 (3.5)	192 (96.5)	NE (NE, NE)	95	0	95 (100)	NE (NE, NE)	NE (NE, NE) 0.9952	0.1706	
1	172	5 (2.9)	167 (97.1)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	1.8159 (0.2105, 15.6666) 0.5874	0.5820	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Metabolism and nutrition disorders; PT: Hyponatraemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.5695
0	199	4 (2.0)	195 (98.0)	NE (NE, NE)	95	1 (1.1)	94 (98.9)	NE (NE, NE)	1.5926 (0.1739, 14.5844) 0.6805	0.6771	
1	172	8 (4.7)	164 (95.3)	NE (NE, NE)	77	4 (5.2)	73 (94.8)	NE (NE, NE)	0.7797 (0.2338, 2.6005) 0.6855	0.6868	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Metabolism and nutrition disorders; PT: Hypercalcaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.7804
0	60	1 (1.7)	59 (98.3)	NE (NE, NE)	31	0	31 (100)	NE (NE, NE)	NE (NE, NE) 0.9979	0.5376	
1	107	6 (5.6)	101 (94.4)	NE (NE, NE)	48	1 (2.1)	47 (97.9)	NE (NE, NE)	2.5412 (0.3055, 21.1405) 0.3882	0.3711	
2	114	3 (2.6)	111 (97.4)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	NE (NE, NE) 0.9958	0.4511	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Metabolism and nutrition disorders; PT: Hypercalcaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	2 (2.2)	88 (97.8)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9977	0.7124	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Metabolism and nutrition disorders; PT: Hyponatraemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.2347
0	60	3 (5.0)	57 (95.0)	NE (NE, NE)	31	0	31 (100)	NE (NE, NE)	NE (NE, NE) 0.9961	0.2143	
1	107	3 (2.8)	104 (97.2)	NE (NE, NE)	48	3 (6.3)	45 (93.8)	NE (NE, NE)	0.3961 (0.0797, 1.9683) 0.2576	0.2407	
2	114	5 (4.4)	109 (95.6)	NE (NE, NE)	50	1 (2.0)	49 (98.0)	NE (NE, NE)	1.6393 (0.1863, 14.4225) 0.6559	0.6536	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Metabolism and nutrition disorders; PT: Hyponatraemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	1 (1.1)	89 (98.9)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	0.4805 (0.0301, 7.6817) 0.6043	0.5961	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypercalcaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.2637
PD	173	5 (2.9)	168 (97.1)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE) 0.9944	0.3119	
PR	48	2 (4.2)	46 (95.8)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	NE (NE, NE) 0.9975	0.4762	
SD	82	1 (1.2)	81 (98.8)	NE (NE, NE)	54	1 (1.9)	53 (98.1)	NE (NE, NE)	0.3930 (0.0232, 6.6446) 0.5174	0.5036	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Metabolism and nutrition disorders; PT: Hyponatraemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.2667
PD	173	8 (4.6)	165 (95.4)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	3.0366 (0.3782, 24.3781)	0.2720	
PR	48	0	48 (100)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	NE (NE, NE)		
SD	82	2 (2.4)	80 (97.6)	NE (NE, NE)	54	3 (5.6)	51 (94.4)	NE (NE, NE)	0.3076 (0.0488, 1.9395)	0.1871	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:37; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_AESOCPT10PAT\_2\_SAS.rtf

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SOC: Metabolism and nutrition disorders; PT: Hypercalcaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.7160
Yes	37	1 (2.7)	36 (97.3)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9984	0.6726	
No	334	11 (3.3)	323 (96.7)	NE (NE, NE)	159	1 (0.6)	158 (99.4)	NE (NE, NE)	3.4036 (0.4297, 26.9580) 0.2460	0.2181	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hyponatraemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.3461
Yes	37	1 (2.7)	36 (97.3)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	0.3376 (0.0211, 5.3999)	0.4202	
No	334	11 (3.3)	323 (96.7)	NE (NE, NE)	159	4 (2.5)	155 (97.5)	NE (NE, NE)	0.4426 (0.3439, 3.4520)	0.8839	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypercalcaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.9998
Yes	24	0	24 (100)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE)		
No	347	12 (3.5)	335 (96.5)	NE (NE, NE)	165	1 (0.6)	164 (99.4)	NE (NE, NE)	3.6738 (0.4682, 28.8249)	0.1855	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hyponatraemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0597
Yes	24	0	24 (100)	NE (NE, NE)	7	1 (14.3)	6 (85.7)	NE (0.1, NE)	0.0000 (0.0000, ) 0.9983	0.0641	
No	347	12 (3.5)	335 (96.5)	NE (NE, NE)	165	4 (2.4)	161 (97.6)	NE (NE, NE)	1.1935 (0.3818, 3.7311) 0.7610	0.7605	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypercalcaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.3499
Normal Function	201	5 (2.5)	196 (97.5)	NE (NE, NE)	80	1 (1.3)	79 (98.8)	NE (NE, NE)	1.0993 (0.1220, 9.9038) 0.9327	0.9327	
Mild Impairment	123	5 (4.1)	118 (95.9)	NE (NE, NE)	65	0	65 (100)	NE (NE, NE)	NE (NE, NE) 0.9960	0.2350	
Moderate Impairment	41	2 (4.9)	39 (95.1)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9967	0.2865	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hyponatraemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.4104
Normal Function	201	7 (3.5)	194 (96.5)	NE (NE, NE)	80	1 (1.3)	79 (98.8)	NE (NE, NE)	2.5566 (0.3136, 20.8455) 0.3806	0.3621	
Mild Impairment	123	3 (2.4)	120 (97.6)	NE (NE, NE)	65	3 (4.6)	62 (95.4)	NE (NE, NE)	0.3405 (0.0653, 1.7757) 0.2010	0.1842	
Moderate Impairment	41	2 (4.9)	39 (95.1)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	1.0768 (0.0975, 11.8857) 0.9519	0.9495	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Metabolism and nutrition disorders; PT: Hypercalcaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.3389
Normal Function	170	4 (2.4)	166 (97.6)	NE (NE, NE)	88	0	88 (100)	NE (NE, NE)	NE (NE, NE) 0.9960	0.2380	
Mild Impairment	194	8 (4.1)	186 (95.9)	NE (NE, NE)	82	1 (1.2)	81 (98.8)	NE (NE, NE)	2.0806 (0.2505, 17.2780) 0.4975	0.4886	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Metabolism and nutrition disorders; PT: Hyponatraemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1752
Normal Function	170	1 (0.6)	169 (99.4)	NE (NE, NE)	88	2 (2.3)	86 (97.7)	NE (NE, NE)	0.2559 (0.0232, 2.8218) 0.2657	0.2297	
Mild Impairment	194	11 (5.7)	183 (94.3)	NE (NE, NE)	82	3 (3.7)	79 (96.3)	NE (NE, NE)	1.2328 (0.3400, 4.4694) 0.7502	0.7475	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypercalcaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.9998
Yes	331	12 (3.6)	319 (96.4)	NE (NE, NE)	146	1 (0.7)	145 (99.3)	NE (NE, NE)	3.5380 (0.4526, 27.6553) 0.2284	0.1993	
No	40	0	40 (100)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hyponatraemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.0868
Yes	331	9 (2.7)	322 (97.3)	NE (NE, NE)	146	5 (3.4)	141 (96.6)	NE (NE, NE)	0.6938 (0.2315, 2.0792) 0.5138	0.5120	
No	40	3 (7.5)	37 (92.5)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9965	0.2521	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypercalcaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.9998
Positive	329	12 (3.6)	317 (96.4)	NE (NE, NE)	152	1 (0.7)	151 (99.3)	NE (NE, NE)	3.6422 (0.4655, 28.4980)	0.2181	0.1881
Negative	42	0	42 (100)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hyponatraemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.2104
Positive	329	10 (3.0)	319 (97.0)	NE (NE, NE)	152	5 (3.3)	147 (96.7)	NE (NE, NE)	0.7553 (0.2558, 2.2307)	0.6109	
Negative	42	2 (4.8)	40 (95.2)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) 0.9968	0.3232	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypercalcaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.9998
Positive	331	12 (3.6)	319 (96.4)	NE (NE, NE)	155	1 (0.6)	154 (99.4)	NE (NE, NE)	3.6967 (0.4723, 28.9322)	0.1825	
Negative	40	0	40 (100)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	0.2130 NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hyponatraemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.2415
Positive	331	10 (3.0)	321 (97.0)	NE (NE, NE)	155	5 (3.2)	150 (96.8)	NE (NE, NE)	0.7684 (0.2602, 2.2692)	0.6330	
Negative	40	2 (5.0)	38 (95.0)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) 0.9969	0.3503	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypomagnesaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.2880
HER2 IHC 1+	214	4 (1.9)	210 (98.1)	NE (NE, NE)	100	4 (4.0)	96 (96.0)	NE (NE, NE)	0.3035 (0.0736, 1.2506) 0.0988	0.0817	
HER2 IHC 2+/ISH Negative	157	6 (3.8)	151 (96.2)	NE (NE, NE)	72	2 (2.8)	70 (97.2)	NE (NE, NE)	0.8022 (0.1544, 4.1687) 0.7932	0.7957	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypomagnesaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.9509
1	220	5 (2.3)	215 (97.7)	NE (NE, NE)	94	3 (3.2)	91 (96.8)	NE (NE, NE)	0.3746 (0.0864, 1.6244) 0.1896	0.1736	
>=2	150	5 (3.3)	145 (96.7)	NE (NE, NE)	78	3 (3.8)	75 (96.2)	NE (7.1, NE)	0.6059 (0.1368, 2.6834) 0.5093	0.5069	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypomagnesaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.5109
Yes	233	7 (3.0)	226 (97.0)	NE (NE, NE)	112	3 (2.7)	109 (97.3)	NE (NE, NE)	0.7811 (0.1945, 3.1362) 0.7276	0.7268	
No	98	2 (2.0)	96 (98.0)	NE (NE, NE)	43	2 (4.7)	41 (95.3)	NE (NE, NE)	0.2198 (0.0309, 1.5661) 0.1305	0.0978	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypomagnesaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2942
<65	289	5 (1.7)	284 (98.3)	NE (NE, NE)	126	4 (3.2)	122 (96.8)	NE (NE, NE)	0.3266 (0.0838, 1.2736) 0.1070	0.0917	
>=65	82	5 (6.1)	77 (93.9)	NE (NE, NE)	46	2 (4.3)	44 (95.7)	NE (NE, NE)	0.9384 (0.1772, 4.9688) 0.9404	0.9421	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypomagnesaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4906
<75	357	9 (2.5)	348 (97.5)	NE (NE, NE)	163	4 (2.5)	159 (97.5)	NE (NE, NE)	0.5943 (0.1766, 1.9998) 0.4007	0.3959	
>=75	14	1 (7.1)	13 (92.9)	NE (NE, NE)	9	2 (22.2)	7 (77.8)	NE (0.3, NE)	0.2622 (0.0234, 2.9406) 0.2777	0.2441	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypomagnesaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.0653
White	175	9 (5.1)	166 (94.9)	NE (NE, NE)	85	3 (3.5)	82 (96.5)	NE (NE, NE)	0.9649 (0.2544, 3.6594) 0.9581	0.9585	
Non-White	196	1 (0.5)	195 (99.5)	NE (NE, NE)	86	3 (3.5)	83 (96.5)	NE (NE, NE)	0.0559 (0.0054, 0.5843) 0.0160	0.0018	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypomagnesaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.0841
Asia	147	0	147 (100)	NE (NE, NE)	63	2 (3.2)	61 (96.8)	NE (NE, NE)	0.0000 (0.0000, ) 0.9973	0.0007	
North America	58	4 (6.9)	54 (93.1)	NE (NE, NE)	28	2 (7.1)	26 (92.9)	NE (NE, NE)	0.7760 (0.1405, 4.2867) 0.7712	0.7719	
Europe + Israel	166	6 (3.6)	160 (96.4)	NE (NE, NE)	81	2 (2.5)	79 (97.5)	NE (NE, NE)	0.8374 (0.1615, 4.3419) 0.8326	0.8324	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypomagnesaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.9837
0	199	5 (2.5)	194 (97.5)	NE (NE, NE)	95	3 (3.2)	92 (96.8)	NE (NE, NE)	0.4907 (0.1131, 2.1296) 0.3418	0.3318	
1	172	5 (2.9)	167 (97.1)	NE (NE, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	0.4331 (0.0979, 1.9164) 0.2702	0.2582	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypomagnesaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.2476
0	60	1 (1.7)	59 (98.3)	NE (NE, NE)	31	1 (3.2)	30 (96.8)	NE (NE, NE)	0.3496 (0.0206, 5.9208) 0.4666	0.4482	
1	107	3 (2.8)	104 (97.2)	NE (NE, NE)	48	0	48 (100)	NE (NE, NE)	NE (NE, NE) 0.9968	0.3687	
2	114	3 (2.6)	111 (97.4)	NE (NE, NE)	50	2 (4.0)	48 (96.0)	NE (NE, NE)	0.3824 (0.0557, 2.6233) 0.3279	0.3114	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypomagnesaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	3 (3.3)	87 (96.7)	NE (NE, NE)	43	3 (7.0)	40 (93.0)	NE (7.1, NE)	0.2581 (0.0469, 1.4203) 0.1196	0.0998	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypomagnesaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.4049
PD	173	6 (3.5)	167 (96.5)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	1.6339 (0.1893, 14.1046)	0.6522	
PR	48	0	48 (100)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	NE (NE, NE)	0.6553	
SD	82	2 (2.4)	80 (97.6)	NE (NE, NE)	54	3 (5.6)	51 (94.4)	NE (NE, NE)	0.3410 (0.0546, 2.1285)	0.2289	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Hypomagnesaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.5478
Yes	37	1 (2.7)	36 (97.3)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	0.1874 (0.0102, 3.4399)	0.2158	
No	334	9 (2.7)	325 (97.3)	NE (NE, NE)	159	5 (3.1)	154 (96.9)	NE (NE, NE)	0.5226 (0.1694, 1.6124)	0.2517	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Metabolism and nutrition disorders; PT: Hypomagnesaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.9997
Yes	24	0	24 (100)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE)		
No	347	10 (2.9)	337 (97.1)	NE (NE, NE)	165	6 (3.6)	159 (96.4)	NE (NE, NE)	0.4664 (0.1636, 1.3296)	0.1451	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Hypomagnesaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0396
Normal Function	201	4 (2.0)	197 (98.0)	NE (NE, NE)	80	4 (5.0)	76 (95.0)	NE (NE, NE)	0.2156 (0.0501, 0.9281) 0.0394	0.0254	
Mild Impairment	123	5 (4.1)	118 (95.9)	NE (NE, NE)	65	0	65 (100)	NE (NE, NE)	NE (NE, NE) 0.9958	0.2151	
Moderate Impairment	41	1 (2.4)	40 (97.6)	NE (NE, NE)	23	2 (8.7)	21 (91.3)	NE (NE, NE)	0.2382 (0.0215, 2.6406) 0.2425	0.2040	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Metabolism and nutrition disorders; PT: Hypomagnesaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.3852
Normal Function	170	5 (2.9)	165 (97.1)	NE (NE, NE)	88	2 (2.3)	86 (97.7)	NE (NE, NE)	0.6467 (0.1199, 3.4888) 0.6123	0.6119	
Mild Impairment	194	5 (2.6)	189 (97.4)	NE (NE, NE)	82	4 (4.9)	78 (95.1)	NE (NE, NE)	0.3538 (0.0913, 1.3715) 0.1329	0.1176	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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DE.T.4.8.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Metabolism and nutrition disorders; PT: Hypomagnesaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1378
Yes	331	8 (2.4)	323 (97.6)	NE (NE, NE)	146	6 (4.1)	140 (95.9)	NE (NE, NE)	0.3529 (0.1185, 1.0511) 0.0614	0.0518	
No	40	2 (5.0)	38 (95.0)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9969	0.3341	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypomagnesaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.6445
Positive	329	9 (2.7)	320 (97.3)	NE (NE, NE)	152	5 (3.3)	147 (96.7)	NE (NE, NE)	0.4988 (0.1618, 1.5378)	0.2179	
Negative	42	1 (2.4)	41 (97.6)	NE (NE, NE)	20	1 (5.0)	19 (95.0)	NE (NE, NE)	0.3006 (0.0173, 5.2140)	0.3847	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Hypomagnesaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.5550
Positive	331	9 (2.7)	322 (97.3)	NE (NE, NE)	155	5 (3.2)	150 (96.8)	NE (NE, NE)	0.5048 (0.1636, 1.5579)	0.2266	
Negative	40	1 (2.5)	39 (97.5)	NE (NE, NE)	17	1 (5.9)	16 (94.1)	NE (NE, NE)	0.2161 (0.0114, 4.1048)	0.2727	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.2126
HER2 IHC 1+	214	110 (51.4)	104 (48.6)	7.6 (5.1, 11.8)	100	42 (42.0)	58 (58.0)	4.4 (2.9, NE)	0.9408 (0.6565, 1.3484) 0.7398	0.7367	
HER2 IHC 2+/ISH Negative	157	69 (43.9)	88 (56.1)	11.8 (7.6, NE)	72	32 (44.4)	40 (55.6)	15.4 (0.9, NE)	0.6522 (0.4253, 1.0001) 0.0500	0.0518	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.3756
1	220	97 (44.1)	123 (55.9)	10.6 (7.6, NE)	94	41 (43.6)	53 (56.4)	7.0 (2.9, NE)	0.7412 (0.5115, 1.0743)	0.1124	
>=2	150	82 (54.7)	68 (45.3)	7.2 (4.1, 11.8)	78	33 (42.3)	45 (57.7)	NE (1.7, NE)	0.9237 (0.6138, 1.3900)	0.7270	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.5127
Yes	233	105 (45.1)	128 (54.9)	11.7 (7.6, 13.8)	112	44 (39.3)	68 (60.7)	15.4 (4.3, NE)	0.8266 (0.5777, 1.1828) 0.2976	0.3051	
No	98	59 (60.2)	39 (39.8)	5.5 (2.8, 8.3)	43	20 (46.5)	23 (53.5)	NE (1.0, NE)	1.0200 (0.6127, 1.6982) 0.9392	0.9470	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Blood and lymphatic system disorders; PT: Any PT

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9216
<65	289	137 (47.4)	152 (52.6)	10.4 (7.2, 13.1)	126	52 (41.3)	74 (58.7)	15.4 (4.1, NE)	0.8311 (0.6009, 1.1496) 0.2637	0.2695	
>=65	82	42 (51.2)	40 (48.8)	7.6 (4.2, 10.6)	46	22 (47.8)	24 (52.2)	7.0 (0.7, NE)	0.7930 (0.4711, 1.3348) 0.3827	0.3850	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8127
<75	357	172 (48.2)	185 (51.8)	9.0 (7.2, 12.1)	163	69 (42.3)	94 (57.7)	7.0 (4.1, NE)	0.8220 (0.6191, 1.0916) 0.1756	0.1796	
>=75	14	7 (50.0)	7 (50.0)	7.6 (0.7, NE)	9	5 (55.6)	4 (44.4)	2.3 (0.3, NE)	0.6272 (0.1962, 2.0048) 0.4314	0.4383	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.6474
White	175	89 (50.9)	86 (49.1)	7.6 (4.1, 12.0)	85	40 (47.1)	45 (52.9)	4.4 (1.0, NE)	0.7640 (0.5230, 1.1161) 0.1640	0.1709	
Non-White	196	90 (45.9)	106 (54.1)	10.4 (7.4, 13.8)	86	34 (39.5)	52 (60.5)	NE (2.9, NE)	0.8501 (0.5701, 1.2677) 0.4257	0.4224	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.5082
Asia	147	66 (44.9)	81 (55.1)	10.4 (7.6, NE)	63	21 (33.3)	42 (66.7)	NE (3.1, NE)	0.9908 (0.6025, 1.6294) 0.9709	0.9524	
North America	58	24 (41.4)	34 (58.6)	11.8 (5.7, NE)	28	11 (39.3)	17 (60.7)	NE (0.5, NE)	0.6298 (0.2987, 1.3276) 0.2242	0.2306	
Europe + Israel	166	89 (53.6)	77 (46.4)	6.9 (3.4, 11.7)	81	42 (51.9)	39 (48.1)	4.2 (0.9, 15.4)	0.7761 (0.5358, 1.1243) 0.1802	0.1862	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.1067
0	199	97 (48.7)	102 (51.3)	8.3 (6.4, 13.1)	95	35 (36.8)	60 (63.2)	15.4 (4.2, NE)	0.9882 (0.6684, 1.4609) 0.9526	0.9551	
1	172	82 (47.7)	90 (52.3)	10.6 (5.6, 12.5)	77	39 (50.6)	38 (49.4)	4.1 (1.0, NE)	0.6408 (0.4338, 0.9466) 0.0254	0.0258	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1452
0	60	27 (45.0)	33 (55.0)	10.4 (4.9, NE)	31	18 (58.1)	13 (41.9)	1.7 (0.3, NE)	0.4196 (0.2226, 0.7909) 0.0072	0.0062	
1	107	54 (50.5)	53 (49.5)	6.2 (3.0, NE)	48	25 (52.1)	23 (47.9)	4.2 (1.4, NE)	0.7972 (0.4951, 1.2836) 0.3510	0.3512	
2	114	59 (51.8)	55 (48.2)	7.6 (5.6, 12.5)	50	19 (38.0)	31 (62.0)	NE (4.1, NE)	1.0330 (0.6110, 1.7463) 0.9036	0.8999	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	39 (43.3)	51 (56.7)	11.8 (8.6, NE)	43	12 (27.9)	31 (72.1)	NE (5.5, NE)	1.0215 (0.5284, 1.9747) 0.9496	0.9466	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.1037
PD	173	83 (48.0)	90 (52.0)	8.3 (5.5, 13.1)	77	33 (42.9)	44 (57.1)	7.0 (2.0, NE)	0.8338 (0.5541, 1.2549)	0.3866	
PR	48	20 (41.7)	28 (58.3)	10.4 (7.6, NE)	21	11 (52.4)	10 (47.6)	1.0 (0.2, NE)	0.4137 (0.1950, 0.8777)	0.0199	
SD	82	43 (52.4)	39 (47.6)	7.4 (2.8, NE)	54	21 (38.9)	33 (61.1)	15.4 (2.9, NE)	1.1407 (0.6730, 1.9335)	0.6263	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.8553
Yes	37	13 (35.1)	24 (64.9)	NE (8.3, NE)	13	4 (30.8)	9 (69.2)	NE (0.3, NE)	0.8001 (0.2531, 2.5289)	0.7159	
No	334	166 (49.7)	168 (50.3)	8.3 (6.4, 11.8)	159	70 (44.0)	89 (56.0)	7.0 (3.1, NE)	0.7041 (0.6205, 1.0928)	0.8234	0.1822
									0.1785		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.9880
Yes	24	8 (33.3)	16 (66.7)	NE (8.3, NE)	7	2 (28.6)	5 (71.4)	NE (0.2, NE)	0.8692 (0.1788, 4.2250) 0.8621	0.8745	
No	347	171 (49.3)	176 (50.7)	8.3 (6.9, 11.8)	165	72 (43.6)	93 (56.4)	7.0 (3.1, NE)	0.8151 (0.6165, 1.0776) 0.1513	0.1545	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.4247
Normal Function	201	93 (46.3)	108 (53.7)	10.6 (6.9, 13.8)	80	34 (42.5)	46 (57.5)	NE (2.3, NE)	0.7341 (0.4915, 1.0965) 0.1310	0.1320	
Mild Impairment	123	62 (50.4)	61 (49.6)	8.6 (6.2, 12.5)	65	23 (35.4)	42 (64.6)	15.4 (4.3, NE)	1.0626 (0.6546, 1.7249) 0.8058	0.7984	
Moderate Impairment	41	22 (53.7)	19 (46.3)	4.2 (0.7, NE)	23	15 (65.2)	8 (34.8)	1.0 (0.3, 7.0)	0.6641 (0.3438, 1.2829) 0.2231	0.2220	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.9869
Normal Function	170	82 (48.2)	88 (51.8)	11.7 (7.6, 13.1)	88	37 (42.0)	51 (58.0)	NE (2.3, NE)	0.8095 (0.5454, 1.2014) 0.2941	0.2995	
Mild Impairment	194	93 (47.9)	101 (52.1)	7.7 (5.5, 12.0)	82	36 (43.9)	46 (56.1)	5.5 (3.1, NE)	0.7897 (0.5348, 1.1662) 0.2352	0.2387	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.7368
Yes	331	162 (48.9)	169 (51.1)	8.6 (6.4, 11.8)	146	64 (43.8)	82 (56.2)	7.0 (3.1, NE)	0.8228 (0.6139, 1.1029) 0.1920	0.1982	
No	40	17 (42.5)	23 (57.5)	12.2 (5.5, NE)	26	10 (38.5)	16 (61.5)	NE (1.0, NE)	0.6875 (0.3055, 1.5473) 0.3653	0.3542	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.0968
Positive	329	164 (49.8)	165 (50.2)	8.3 (6.4, 11.8)	152	64 (42.1)	88 (57.9)	7.0 (4.1, NE)	0.8852 (0.6608, 1.1857)	0.4202	
Negative	42	15 (35.7)	27 (64.3)	10.6 (7.6, NE)	20	10 (50.0)	10 (50.0)	2.9 (0.3, NE)	0.4134 (0.1461, 0.8458)	0.0154	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.0229
Positive	331	165 (49.8)	166 (50.2)	8.3 (6.2, 11.8)	155	64 (41.3)	91 (58.7)	15.4 (4.2, NE)	0.9061 (0.6766, 1.2134)	0.5161	
Negative	40	14 (35.0)	26 (65.0)	10.6 (7.6, NE)	17	10 (58.8)	7 (41.2)	1.0 (0.3, NE)	0.2474 (0.0979, 0.6251)	0.0016	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0434
HER2 IHC 1+	214	83 (38.8)	131 (61.2)	16.1 (10.4, NE)	100	21 (21.0)	79 (79.0)	NE (NE, NE)	1.5226 (0.9378, 2.4722) 0.0891	0.0893	
HER2 IHC 2+/ISH Negative	157	56 (35.7)	101 (64.3)	24.8 (10.4, NE)	72	24 (33.3)	48 (66.7)	15.4 (15.4, NE)	0.7241 (0.4445, 1.1796) 0.1948	0.1953	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.8388
1	220	77 (35.0)	143 (65.0)	NE (10.6, NE)	94	23 (24.5)	71 (75.5)	15.4 (15.4, NE)	1.1127 (0.6939, 1.7843) 0.6576	0.6662	
>=2	150	62 (41.3)	88 (58.7)	12.2 (8.6, NE)	78	22 (28.2)	56 (71.8)	NE (NE, NE)	1.0791 (0.6578, 1.7700) 0.7631	0.7564	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.7264
Yes	233	78 (33.5)	155 (66.5)	NE (11.8, NE)	112	25 (22.3)	87 (77.7)	15.4 (15.4, NE)	1.0793 (0.6810, 1.7107) 0.7454	0.7487	
No	98	48 (49.0)	50 (51.0)	7.6 (4.2, NE)	43	14 (32.6)	29 (67.4)	NE (2.9, NE)	1.3394 (0.7361, 2.4372) 0.3387	0.3401	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7216
<65	289	106 (36.7)	183 (63.3)	24.8 (11.8, NE)	126	32 (25.4)	94 (74.6)	NE (15.4, NE)	1.0819 (0.7238, 1.6171) 0.7011	0.7061	
>=65	82	33 (40.2)	49 (59.8)	11.7 (7.4, NE)	46	13 (28.3)	33 (71.7)	NE (7.0, NE)	1.1263 (0.5870, 2.1611) 0.7206	0.7234	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7284
<75	357	132 (37.0)	225 (63.0)	24.8 (11.7, NE)	163	41 (25.2)	122 (74.8)	NE (15.4, NE)	1.1197 (0.7844, 1.5983) 0.5335	0.5402	
>=75	14	7 (50.0)	7 (50.0)	7.6 (1.4, 16.1)	9	4 (44.4)	5 (55.6)	NE (0.3, NE)	0.7336 (0.2034, 2.6453) 0.6359	0.6514	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.7842
White	175	64 (36.6)	111 (63.4)	NE (11.8, NE)	85	22 (25.9)	63 (74.1)	15.4 (15.4, NE)	1.0388 (0.6338, 1.7027) 0.8800	0.8769	
Non-White	196	75 (38.3)	121 (61.7)	24.8 (9.0, NE)	86	23 (26.7)	63 (73.3)	NE (7.0, NE)	1.1143 (0.6943, 1.7884) 0.6539	0.6655	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.2481
Asia	147	63 (42.9)	84 (57.1)	10.6 (7.6, NE)	63	16 (25.4)	47 (74.6)	NE (NE, NE)	1.3264 (0.7612, 2.3113) 0.3188	0.3276	
North America	58	18 (31.0)	40 (69.0)	NE (11.8, NE)	28	9 (32.1)	19 (67.9)	NE (0.5, NE)	0.6462 (0.2814, 1.4841) 0.3034	0.3046	
Europe + Israel	166	58 (34.9)	108 (65.1)	NE (11.7, NE)	81	20 (24.7)	61 (75.3)	15.4 (7.0, NE)	1.0941 (0.6531, 1.8326) 0.7327	0.7332	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.2060
0	199	80 (40.2)	119 (59.8)	12.2 (8.6, NE)	95	22 (23.2)	73 (76.8)	NE (15.4, NE)	1.3060 (0.8099, 2.1059) 0.2735	0.2730	
1	172	59 (34.3)	113 (65.7)	24.8 (11.8, 24.8)	77	23 (29.9)	54 (70.1)	NE (5.5, NE)	0.8960 (0.5484, 1.4639) 0.6611	0.6608	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1834
0	60	22 (36.7)	38 (63.3)	10.6 (6.6, NE)	31	12 (38.7)	19 (61.3)	2.9 (2.0, NE)	0.6028 (0.2927, 1.2417) 0.1698	0.1647	
1	107	46 (43.0)	61 (57.0)	NE (5.4, NE)	48	18 (37.5)	30 (62.5)	15.4 (4.2, NE)	1.0159 (0.5875, 1.7567) 0.9550	0.9600	
2	114	41 (36.0)	73 (64.0)	NE (11.7, NE)	50	7 (14.0)	43 (86.0)	NE (NE, NE)	2.0911 (0.9289, 4.7075) 0.0748	0.0693	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	30 (33.3)	60 (66.7)	24.8 (11.8, NE)	43	8 (18.6)	35 (81.4)	NE (NE, NE)	1.1068 (0.4953, 2.4736) 0.8046	0.8017	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.1365
PD	173	64 (37.0)	109 (63.0)	NE (8.3, NE)	77	20 (26.0)	57 (74.0)	NE (7.0, NE)	1.1408 (0.6867, 1.8953)	0.6135	
PR	48	15 (31.3)	33 (68.8)	24.8 (9.9, 24.8)	21	7 (33.3)	14 (66.7)	NE (0.7, NE)	0.5098 (0.2024, 1.2845)	0.1489	
SD	82	35 (42.7)	47 (57.3)	11.8 (6.2, NE)	54	11 (20.4)	43 (79.6)	NE (15.4, NE)	1.8322 (0.9243, 3.6319)	0.0820	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.8831
Yes	37	10 (27.0)	27 (73.0)	NE (10.4, NE)	13	2 (15.4)	11 (84.6)	NE (NE, NE)	1.2581 (0.2671, 5.9261)	0.7710	
No	334	129 (38.6)	205 (61.4)	16.1 (10.6, NE)	159	43 (27.0)	116 (73.0)	NE (15.4, NE)	1.0928 (0.7699, 1.5512)	0.6233	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.7080
Yes	24	7 (29.2)	17 (70.8)	NE (8.3, NE)	7	2 (28.6)	5 (71.4)	NE (0.7, NE)	0.8816 (0.1754, 4.4309) 0.8784	0.8783	
No	347	132 (38.0)	215 (62.0)	24.8 (11.7, NE)	165	43 (26.1)	122 (73.9)	NE (15.4, NE)	1.1016 (0.7768, 1.5623) 0.5871	0.5906	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.5736
Normal Function	201	70 (34.8)	131 (65.2)	NE (11.7, NE)	80	18 (22.5)	62 (77.5)	NE (NE, NE)	1.0969 (0.6475, 1.8584) 0.7309	0.7324	
Mild Impairment	123	48 (39.0)	75 (61.0)	24.8 (7.7, 24.8)	65	14 (21.5)	51 (78.5)	15.4 (15.4, NE)	1.3985 (0.7645, 2.5582) 0.2764	0.2757	
Moderate Impairment	41	19 (46.3)	22 (53.7)	16.1 (2.0, NE)	23	11 (47.8)	12 (52.2)	7.0 (1.0, NE)	0.8699 (0.4104, 1.8438) 0.7161	0.7102	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.7572
Normal Function	170	64 (37.6)	106 (62.4)	24.8 (11.7, NE)	88	22 (25.0)	66 (75.0)	NE (NE, NE)	1.1812 (0.7221, 1.9323) 0.5071	0.5092	
Mild Impairment	194	71 (36.6)	123 (63.4)	12.1 (8.3, NE)	82	22 (26.8)	60 (73.2)	15.4 (7.0, NE)	0.9803 (0.6025, 1.5949) 0.9361	0.9351	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.5313
Yes	331	125 (37.8)	206 (62.2)	24.8 (10.4, NE)	146	38 (26.0)	108 (74.0)	NE (15.4, NE)	1.1197 (0.7749, 1.6181) 0.5472	0.5507	
No	40	14 (35.0)	26 (65.0)	NE (6.9, NE)	26	7 (26.9)	19 (73.1)	NE (2.3, NE)	0.9245 (0.3639, 2.3492) 0.8690	0.8582	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.3618
Positive	329	126 (38.3)	203 (61.7)	24.8 (11.7, NE)	152	39 (25.7)	113 (74.3)	NE (15.4, NE)	1.1643 (0.8091, 1.6754)	0.4171	
Negative	42	13 (31.0)	29 (69.0)	12.2 (7.6, NE)	20	6 (30.0)	14 (70.0)	NE (2.0, NE)	0.5381 (0.1885, 1.5363)	0.2415	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.1534
Positive	331	127 (38.4)	204 (61.6)	24.8 (11.7, NE)	155	39 (25.2)	116 (74.8)	NE (15.4, NE)	1.1946 (0.8304, 1.7185)	0.3411	
Negative	40	12 (30.0)	28 (70.0)	12.2 (10.4, NE)	17	6 (35.3)	11 (64.7)	NE (1.0, NE)	0.3914 (0.1318, 1.1622)	0.0812	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.6386
HER2 IHC 1+	214	31 (14.5)	183 (85.5)	NE (NE, NE)	100	21 (21.0)	79 (79.0)	NE (NE, NE)	0.5199 (0.2963, 0.9124) 0.0226	0.0210	
HER2 IHC 2+/ISH Negative	157	18 (11.5)	139 (88.5)	NE (NE, NE)	72	10 (13.9)	62 (86.1)	NE (NE, NE)	0.6734 (0.3082, 1.4712) 0.3213	0.3206	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.3693
1	220	26 (11.8)	194 (88.2)	NE (NE, NE)	94	18 (19.1)	76 (80.9)	NE (NE, NE)	0.4932 (0.2685, 0.9058) 0.0227	0.0208	
>=2	150	23 (15.3)	127 (84.7)	NE (NE, NE)	78	13 (16.7)	65 (83.3)	NE (NE, NE)	0.6994 (0.3509, 1.3939) 0.3096	0.3089	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.6062
Yes	233	31 (13.3)	202 (86.7)	NE (NE, NE)	112	19 (17.0)	93 (83.0)	NE (NE, NE)	0.5963 (0.3332, 1.0670) 0.0816	0.0803	
No	98	16 (16.3)	82 (83.7)	NE (NE, NE)	43	7 (16.3)	36 (83.7)	NE (NE, NE)	0.7944 (0.3250, 1.9417) 0.6137	0.6138	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9349
<65	289	37 (12.8)	252 (87.2)	NE (NE, NE)	126	22 (17.5)	104 (82.5)	NE (NE, NE)	0.5598 (0.3273, 0.9577) 0.0342	0.0328	
>=65	82	12 (14.6)	70 (85.4)	NE (NE, NE)	46	9 (19.6)	37 (80.4)	NE (NE, NE)	0.6218 (0.2614, 1.4794) 0.2827	0.2847	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0262
<75	357	46 (12.9)	311 (87.1)	NE (NE, NE)	163	31 (19.0)	132 (81.0)	NE (NE, NE)	0.5218 (0.3286, 0.8286) 0.0058	0.0053	
>=75	14	3 (21.4)	11 (78.6)	NE (3.4, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9973	0.1603	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.5511
White	175	34 (19.4)	141 (80.6)	NE (NE, NE)	85	20 (23.5)	65 (76.5)	NE (NE, NE)	0.6376 (0.3652, 1.1132) 0.1135	0.1124	
Non-White	196	15 (7.7)	181 (92.3)	NE (NE, NE)	86	11 (12.8)	75 (87.2)	NE (NE, NE)	0.4494 (0.2021, 0.9995) 0.0499	0.0450	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.5908
Asia	147	5 (3.4)	142 (96.6)	NE (NE, NE)	63	3 (4.8)	60 (95.2)	NE (NE, NE)	0.5614 (0.1281, 2.4602) 0.4438	0.4400	
North America	58	1 (1.7)	57 (98.3)	NE (NE, NE)	28	2 (7.1)	26 (92.9)	NE (NE, NE)	0.0000 (0.0000, ) 0.9968	0.0381	
Europe + Israel	166	43 (25.9)	123 (74.1)	NE (NE, NE)	81	26 (32.1)	55 (67.9)	NE (NE, NE)	0.6159 (0.3770, 1.0064) 0.0530	0.0528	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.0896
0	199	27 (13.6)	172 (86.4)	NE (NE, NE)	95	12 (12.6)	83 (87.4)	NE (NE, NE)	0.8268 (0.4157, 1.6442) 0.5876	0.5902	
1	172	22 (12.8)	150 (87.2)	NE (NE, NE)	77	19 (24.7)	58 (75.3)	NE (NE, NE)	0.4026 (0.2155, 0.7520) 0.0043	0.0033	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.7096
0	60	9 (15.0)	51 (85.0)	NE (NE, NE)	31	8 (25.8)	23 (74.2)	NE (NE, NE)	0.4435 (0.1688, 1.1653) 0.0990	0.0918	
1	107	12 (11.2)	95 (88.8)	NE (NE, NE)	48	10 (20.8)	38 (79.2)	NE (NE, NE)	0.4540 (0.1956, 1.0538) 0.0661	0.0604	
2	114	21 (18.4)	93 (81.6)	NE (NE, NE)	50	10 (20.0)	40 (80.0)	NE (NE, NE)	0.6896 (0.3198, 1.4869) 0.3431	0.3424	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	7 (7.8)	83 (92.2)	NE (NE, NE)	43	3 (7.0)	40 (93.0)	NE (NE, NE)	0.8250 (0.2088, 3.2598) 0.7838	0.7835	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.5443
PD	173	26 (15.0)	147 (85.0)	NE (NE, NE)	77	16 (20.8)	61 (79.2)	NE (NE, NE)	0.5260 (0.2785, 0.9937)	0.0450	
PR	48	6 (12.5)	42 (87.5)	NE (NE, NE)	21	5 (23.8)	16 (76.2)	NE (NE, NE)	0.3777 (0.1136, 1.2553)	0.1019	
SD	82	13 (15.9)	69 (84.1)	NE (NE, NE)	54	9 (16.7)	45 (83.3)	NE (NE, NE)	0.8144 (0.3465, 1.9137)	0.6423	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.9342
Yes	37	4 (10.8)	33 (89.2)	NE (NE, NE)	13	2 (15.4)	11 (84.6)	NE (1.0, NE)	0.6421 (0.1176, 3.5072)	0.6065	
No	334	45 (13.5)	289 (86.5)	NE (NE, NE)	159	29 (18.2)	130 (81.8)	NE (NE, NE)	0.5735 (0.3575, 0.9200)	0.0203	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.8565
Yes	24	2 (8.3)	22 (91.7)	NE (NE, NE)	7	1 (14.3)	6 (85.7)	NE (0.3, NE)	0.5343 (0.0484, 5.8986) 0.6089	0.6031	
No	347	47 (13.5)	300 (86.5)	NE (NE, NE)	165	30 (18.2)	135 (81.8)	NE (NE, NE)	0.5777 (0.3632, 0.9187) 0.0204	0.0196	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.7522
Normal Function	201	26 (12.9)	175 (87.1)	NE (NE, NE)	80	16 (20.0)	64 (80.0)	NE (NE, NE)	0.4634 (0.2445, 0.8785) 0.0184	0.0163	
Mild Impairment	123	16 (13.0)	107 (87.0)	NE (NE, NE)	65	11 (16.9)	54 (83.1)	NE (NE, NE)	0.6320 (0.2913, 1.3712) 0.2456	0.2446	
Moderate Impairment	41	7 (17.1)	34 (82.9)	NE (NE, NE)	23	4 (17.4)	19 (82.6)	NE (NE, NE)	0.8350 (0.2439, 2.8578) 0.7739	0.7837	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1226
Normal Function	170	20 (11.8)	150 (88.2)	NE (NE, NE)	88	19 (21.6)	69 (78.4)	NE (NE, NE)	0.4036 (0.2128, 0.7655) 0.0055	0.0043	
Mild Impairment	194	29 (14.9)	165 (85.1)	NE (NE, NE)	82	12 (14.6)	70 (85.4)	NE (NE, NE)	0.8255 (0.4187, 1.6273) 0.5797	0.5802	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.5378
Yes	331	46 (13.9)	285 (86.1)	NE (NE, NE)	146	27 (18.5)	119 (81.5)	NE (NE, NE)	0.5950 (0.3682, 0.9615) 0.0340	0.0333	
No	40	3 (7.5)	37 (92.5)	NE (NE, NE)	26	4 (15.4)	22 (84.6)	NE (NE, NE)	0.2893 (0.0566, 1.4794) 0.1363	0.1158	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.1596
Positive	329	47 (14.3)	282 (85.7)	NE (NE, NE)	152	27 (17.8)	125 (82.2)	NE (NE, NE)	0.6234 (0.3862, 1.0062)	0.0525	
Negative	42	2 (4.8)	40 (95.2)	NE (NE, NE)	20	4 (20.0)	16 (80.0)	NE (NE, NE)	0.2250 (0.0412, 1.2291)	0.0604	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.0427
Positive	331	47 (14.2)	284 (85.8)	NE (NE, NE)	155	26 (16.8)	129 (83.2)	NE (NE, NE)	0.6586 (0.4057, 1.0693)	0.0913	
Negative	40	2 (5.0)	38 (95.0)	NE (NE, NE)	17	5 (29.4)	12 (70.6)	NE (0.9, NE)	0.1550 (0.0300, 0.7996)	0.0107	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.6906
HER2 IHC 1+	214	14 (6.5)	200 (93.5)	NE (NE, NE)	100	2 (2.0)	98 (98.0)	NE (NE, NE)	2.1329 (0.4753, 9.5717) 0.3227	0.3116	
HER2 IHC 2+/ISH Negative	157	9 (5.7)	148 (94.3)	NE (NE, NE)	72	2 (2.8)	70 (97.2)	NE (16.1, NE)	1.3376 (0.2807, 6.3734) 0.7150	0.7158	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.8711
1	220	13 (5.9)	207 (94.1)	NE (NE, NE)	94	2 (2.1)	92 (97.9)	NE (16.1, NE)	1.8422 (0.4080, 8.3185) 0.4270	0.4197	
>=2	150	10 (6.7)	140 (93.3)	NE (NE, NE)	78	2 (2.6)	76 (97.4)	NE (NE, NE)	1.6452 (0.3489, 7.7572) 0.5292	0.5252	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.1742
Yes	233	16 (6.9)	217 (93.1)	NE (NE, NE)	112	3 (2.7)	109 (97.3)	NE (16.1, NE)	1.4829 (0.4197, 5.2387) 0.5406	0.5377	
No	98	6 (6.1)	92 (93.9)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9951	0.1554	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5377
<65	289	21 (7.3)	268 (92.7)	NE (NE, NE)	126	3 (2.4)	123 (97.6)	NE (16.1, NE)	1.8249 (0.5330, 6.2483) 0.3381	0.3311	
>=65	82	2 (2.4)	80 (97.6)	NE (NE, NE)	46	1 (2.2)	45 (97.8)	NE (NE, NE)	1.0848 (0.0983, 11.9733) 0.9471	0.9470	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0874
<75	357	23 (6.4)	334 (93.6)	NE (NE, NE)	163	3 (1.8)	160 (98.2)	NE (16.1, NE)	2.1866 (0.6448, 7.4154) 0.2092	0.1983	
>=75	14	0	14 (100)	NE (NE, NE)	9	1 (11.1)	8 (88.9)	NE (0.3, NE)	0.0000 (0.0000, ) 0.9984	0.2123	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.8358
White	175	18 (10.3)	157 (89.7)	NE (NE, NE)	85	3 (3.5)	82 (96.5)	NE (16.1, NE)	1.6886 (0.4854, 5.8739) 0.4101	0.4051	
Non-White	196	5 (2.6)	191 (97.4)	NE (NE, NE)	86	1 (1.2)	85 (98.8)	NE (NE, NE)	1.8823 (0.2181, 16.2446) 0.5652	0.5579	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.9574
Asia	147	0	147 (100)	NE (NE, NE)	63	0	63 (100)	NE (NE, NE)	NE (NE, NE)		
North America	58	5 (8.6)	53 (91.4)	NE (NE, NE)	28	1 (3.6)	27 (96.4)	NE (NE, NE)	1.0219 (0.1029, 10.1477) 0.9852	0.9851	
Europe + Israel	166	18 (10.8)	148 (89.2)	NE (NE, NE)	81	3 (3.7)	78 (96.3)	NE (16.1, NE)	2.0707 (0.6010, 7.1339) 0.2488	0.2395	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.4869
0	199	13 (6.5)	186 (93.5)	NE (NE, NE)	95	3 (3.2)	92 (96.8)	NE (16.1, NE)	1.4194 (0.3969, 5.0761) 0.5901	0.5880	
1	172	10 (5.8)	162 (94.2)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	2.5243 (0.3120, 20.4264) 0.3854	0.3695	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1555
0	60	5 (8.3)	55 (91.7)	NE (NE, NE)	31	2 (6.5)	29 (93.5)	NE (NE, NE)	0.9527 (0.1771, 5.1252) 0.9550	0.9566	
1	107	6 (5.6)	101 (94.4)	NE (NE, NE)	48	1 (2.1)	47 (97.9)	NE (16.1, NE)	2.1437 (0.2555, 17.9882) 0.4823	0.4724	
2	114	11 (9.6)	103 (90.4)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	NE (NE, NE) 0.9918	0.1374	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	1 (1.1)	89 (98.9)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	0.4333 (0.0270, 6.9506) 0.5548	0.5432	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.6311
PD	173	12 (6.9)	161 (93.1)	NE (NE, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	1.3655 (0.3788, 4.9219)	0.6320	
PR	48	2 (4.2)	46 (95.8)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	NE (NE, NE) 0.9976	0.5104	
SD	82	5 (6.1)	77 (93.9)	NE (NE, NE)	54	1 (1.9)	53 (98.1)	NE (16.1, NE)	1.7684 (0.2006, 15.5886) 0.6077	0.6031	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.3768
Yes	37	3 (8.1)	34 (91.9)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9973	0.4610	
No	334	20 (6.0)	314 (94.0)	NE (NE, NE)	159	4 (2.5)	155 (97.5)	NE (16.1, NE)	1.5609 (0.5233, 4.6561) 0.4246	0.4210	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0294
Yes	24	0	24 (100)	NE (NE, NE)	7	1 (14.3)	6 (85.7)	NE (0.2, NE)	0.0000 (0.0000, ) 0.9983	0.0641	
No	347	23 (6.6)	324 (93.4)	NE (NE, NE)	165	3 (1.8)	162 (98.2)	NE (16.1, NE)	2.3231 (0.6861, 7.8663) 0.1756	0.1638	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.4197
Normal Function	201	15 (7.5)	186 (92.5)	NE (NE, NE)	80	1 (1.3)	79 (98.8)	NE (NE, NE)	3.4038 (0.4409, 26.2764) 0.2401	0.2119	
Mild Impairment	123	7 (5.7)	116 (94.3)	NE (NE, NE)	65	2 (3.1)	63 (96.9)	16.1 (16.1, NE)	1.1571 (0.2279, 5.8753) 0.8603	0.8612	
Moderate Impairment	41	1 (2.4)	40 (97.6)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	0.5582 (0.0349, 8.9275) 0.6802	0.6761	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.9938
Normal Function	170	5 (2.9)	165 (97.1)	NE (NE, NE)	88	1 (1.1)	87 (98.9)	NE (NE, NE)	1.3049 (0.1441, 11.8195) 0.8129	0.8123	
Mild Impairment	194	18 (9.3)	176 (90.7)	NE (NE, NE)	82	3 (3.7)	79 (96.3)	16.1 (16.1, NE)	1.6907 (0.4891, 5.8449) 0.4067	0.4014	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.2216
Yes	331	22 (6.6)	309 (93.4)	NE (NE, NE)	146	3 (2.1)	143 (97.9)	NE (16.1, NE)	2.2015 (0.6506, 7.4497) 0.2045	0.1933	
No	40	1 (2.5)	39 (97.5)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	0.1645 (0.0052, 5.1920) 0.3055	0.2823	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.2018
Positive	329	22 (6.7)	307 (93.3)	NE (NE, NE)	152	3 (2.0)	149 (98.0)	NE (16.1, NE)	2.1628 (0.6378, 7.3339)	0.2048	
Negative	42	1 (2.4)	41 (97.6)	NE (NE, NE)	20	1 (5.0)	19 (95.0)	NE (NE, NE)	0.2156 (0.0301, 7.7061)	0.5978	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.1699
Positive	331	22 (6.6)	309 (93.4)	NE (NE, NE)	155	3 (1.9)	152 (98.1)	NE (16.1, NE)	2.1922 (0.6463, 7.4359)	0.1968	
Negative	40	1 (2.5)	39 (97.5)	NE (NE, NE)	17	1 (5.9)	16 (94.1)	NE (NE, NE)	0.4305 (0.0269, 6.8829)	0.5393	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Blood and lymphatic system disorders; PT: Leukopenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.4042
HER2 IHC 1+	214	8 (3.7)	206 (96.3)	NE (NE, NE)	100	3 (3.0)	97 (97.0)	NE (NE, NE)	1.0655 (0.2799, 4.0562) 0.9259	0.9259	
HER2 IHC 2+/ISH Negative	157	5 (3.2)	152 (96.8)	NE (NE, NE)	72	4 (5.6)	68 (94.4)	NE (NE, NE)	0.4585 (0.1202, 1.7492) 0.2537	0.2425	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Leukopenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.9801
1	220	8 (3.6)	212 (96.4)	NE (NE, NE)	94	4 (4.3)	90 (95.7)	NE (NE, NE)	0.7653 (0.2299, 2.5476) 0.6628	0.6622	
>=2	150	5 (3.3)	145 (96.7)	NE (NE, NE)	78	3 (3.8)	75 (96.2)	NE (NE, NE)	0.6230 (0.1419, 2.7349) 0.5307	0.5273	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Blood and lymphatic system disorders; PT: Leukopenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.3791
Yes	233	6 (2.6)	227 (97.4)	NE (NE, NE)	112	5 (4.5)	107 (95.5)	NE (NE, NE)	0.5387 (0.1642, 1.7673) 0.3075	0.3000	
No	98	6 (6.1)	92 (93.9)	NE (NE, NE)	43	2 (4.7)	41 (95.3)	NE (NE, NE)	0.9824 (0.1958, 4.9293) 0.9828	0.9828	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Blood and lymphatic system disorders; PT: Leukopenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8323
<65	289	9 (3.1)	280 (96.9)	NE (NE, NE)	126	4 (3.2)	122 (96.8)	NE (NE, NE)	0.8052 (0.2450, 2.6467) 0.7212	0.7209	
>=65	82	4 (4.9)	78 (95.1)	NE (NE, NE)	46	3 (6.5)	43 (93.5)	NE (NE, NE)	0.6096 (0.1332, 2.7903) 0.5236	0.5197	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Leukopenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2412
<75	357	12 (3.4)	345 (96.6)	NE (NE, NE)	163	7 (4.3)	156 (95.7)	NE (NE, NE)	0.6286 (0.2438, 1.6202) 0.3365	0.3330	
>=75	14	1 (7.1)	13 (92.9)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9984	0.4054	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Leukopenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.6988
White	175	6 (3.4)	169 (96.6)	NE (NE, NE)	85	4 (4.7)	81 (95.3)	NE (NE, NE)	0.5230 (0.1423, 1.9216) 0.3289	0.3214	
Non-White	196	7 (3.6)	189 (96.4)	NE (NE, NE)	86	3 (3.5)	83 (96.5)	NE (NE, NE)	0.9332 (0.2403, 3.6238) 0.9204	0.9222	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Leukopenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.9369
Asia	147	3 (2.0)	144 (98.0)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (NE, NE)	1.0038 (0.1030, 9.7838) 0.9974	0.9974	
North America	58	0	58 (100)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) NE		
Europe + Israel	166	10 (6.0)	156 (94.0)	NE (NE, NE)	81	6 (7.4)	75 (92.6)	NE (NE, NE)	0.6799 (0.2438, 1.8959) 0.4609	0.4584	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Leukopenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.1510
0	199	5 (2.5)	194 (97.5)	NE (NE, NE)	95	5 (5.3)	90 (94.7)	NE (NE, NE)	0.3724 (0.1062, 1.3058) 0.1228	0.1088	
1	172	8 (4.7)	164 (95.3)	NE (NE, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	1.5507 (0.3241, 7.4202) 0.5828	0.5789	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Leukopenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1198
0	60	4 (6.7)	56 (93.3)	NE (NE, NE)	31	0	31 (100)	NE (NE, NE)	NE (NE, NE) 0.9960	0.2322	
1	107	3 (2.8)	104 (97.2)	NE (NE, NE)	48	2 (4.2)	46 (95.8)	NE (NE, NE)	0.6503 (0.1086, 3.8941) 0.6375	0.6350	
2	114	3 (2.6)	111 (97.4)	NE (NE, NE)	50	4 (8.0)	46 (92.0)	NE (NE, NE)	0.3095 (0.0693, 1.3833) 0.1247	0.1049	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Leukopenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	3 (3.3)	87 (96.7)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	0.8755 (0.0841, 9.1195) 0.9115	0.9114	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Leukopenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.5941
PD	173	6 (3.5)	167 (96.5)	NE (NE, NE)	77	4 (5.2)	73 (94.8)	NE (NE, NE)	0.5903 (0.1659, 2.1004)	0.4105	
PR	48	1 (2.1)	47 (97.9)	NE (NE, NE)	21	1 (4.8)	20 (95.2)	NE (NE, NE)	0.4156 (0.0118, 4.0380)	0.2704	
SD	82	3 (3.7)	79 (96.3)	NE (NE, NE)	54	1 (1.9)	53 (98.1)	NE (NE, NE)	0.3066 (0.2015, 18.6242)	0.5599	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Leukopenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.0966
Yes	37	0	37 (100)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	0.0000 (0.0000, )	0.0916	
No	334	13 (3.9)	321 (96.1)	NE (NE, NE)	159	6 (3.8)	153 (96.2)	NE (NE, NE)	0.8511 (0.3199, 2.2640)	0.7471	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Leukopenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.9999
Yes	24	0	24 (100)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE)		
No	347	13 (3.7)	334 (96.3)	NE (NE, NE)	165	7 (4.2)	158 (95.8)	NE (NE, NE)	0.7239 (0.2855, 1.8357) 0.4962	0.4950	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Leukopenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.4790
Normal Function	201	9 (4.5)	192 (95.5)	NE (NE, NE)	80	4 (5.0)	76 (95.0)	NE (NE, NE)	0.7386 (0.2248, 2.4271) 0.6176	0.6170	
Mild Impairment	123	3 (2.4)	120 (97.6)	NE (NE, NE)	65	3 (4.6)	62 (95.4)	NE (NE, NE)	0.3779 (0.0701, 2.0378) 0.2577	0.2410	
Moderate Impairment	41	1 (2.4)	40 (97.6)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9977	0.4742	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Leukopenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.0382
Normal Function	170	7 (4.1)	163 (95.9)	NE (NE, NE)	88	1 (1.1)	87 (98.9)	NE (NE, NE)	2.9025 (0.3525, 23.8978) 0.3219	0.2996	
Mild Impairment	194	6 (3.1)	188 (96.9)	NE (NE, NE)	82	6 (7.3)	76 (92.7)	NE (NE, NE)	0.3502 (0.1111, 1.1040) 0.0733	0.0616	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Leukopenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1281
Yes	331	11 (3.3)	320 (96.7)	NE (NE, NE)	146	7 (4.8)	139 (95.2)	NE (NE, NE)	0.5791 (0.2219, 1.5113) 0.2643	0.2593	
No	40	2 (5.0)	38 (95.0)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9969	0.3385	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Leukopenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.3285
Positive	329	12 (3.6)	317 (96.4)	NE (NE, NE)	152	7 (4.6)	145 (95.4)	NE (NE, NE)	0.6430 (0.2502, 1.6521)	0.3559	
Negative	42	1 (2.4)	41 (97.6)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) 0.9978	0.4902	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Leukopenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.3576
Positive	331	12 (3.6)	319 (96.4)	NE (NE, NE)	155	7 (4.5)	148 (95.5)	NE (NE, NE)	0.6532 (0.2542, 1.6785)	0.3736	
Negative	40	1 (2.5)	39 (97.5)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) 0.9978	0.5145	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.8091
HER2 IHC 1+	214	88 (41.1)	126 (58.9)	15.2 (11.0, NE)	100	28 (28.0)	72 (72.0)	NE (NE, NE)	1.0790 (0.7003, 1.6624) 0.7304	0.7278	
HER2 IHC 2+/ISH Negative	157	67 (42.7)	90 (57.3)	13.8 (8.5, 24.4)	72	22 (30.6)	50 (69.4)	NE (8.3, NE)	0.9564 (0.5851, 1.5634) 0.8590	0.8618	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.3408
1	220	91 (41.4)	129 (58.6)	17.9 (11.0, 24.4)	94	24 (25.5)	70 (74.5)	NE (NE, NE)	1.1947 (0.7573, 1.8848) 0.4444	0.4421	
>=2	150	63 (42.0)	87 (58.0)	14.3 (10.5, 17.1)	78	26 (33.3)	52 (66.7)	8.3 (4.1, NE)	0.8427 (0.5272, 1.3471) 0.4747	0.4712	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.8939
Yes	233	101 (43.3)	132 (56.7)	11.8 (8.5, 17.9)	112	33 (29.5)	79 (70.5)	NE (NE, NE)	1.0280 (0.6885, 1.5349) 0.8925	0.8892	
No	98	34 (34.7)	64 (65.3)	23.3 (15.0, NE)	43	11 (25.6)	32 (74.4)	NE (8.3, NE)	0.9894 (0.4964, 1.9717) 0.9757	0.9760	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2891
<65	289	119 (41.2)	170 (58.8)	15.0 (11.8, 23.3)	126	32 (25.4)	94 (74.6)	NE (8.3, NE)	1.1649 (0.7833, 1.7323) 0.4510	0.4508	
>=65	82	36 (43.9)	46 (56.1)	12.6 (7.0, NE)	46	18 (39.1)	28 (60.9)	NE (2.9, NE)	0.7828 (0.4395, 1.3942) 0.4056	0.4050	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2933
<75	357	148 (41.5)	209 (58.5)	14.7 (11.8, 20.4)	163	48 (29.4)	115 (70.6)	NE (8.3, NE)	0.9843 (0.7060, 1.3723) 0.9256	0.9261	
>=75	14	7 (50.0)	7 (50.0)	6.9 (3.3, NE)	9	2 (22.2)	7 (77.8)	NE (0.0, NE)	2.0900 (0.4332, 10.0847) 0.3586	0.3478	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.1084
White	175	85 (48.6)	90 (51.4)	10.5 (5.0, 17.9)	85	23 (27.1)	62 (72.9)	NE (NE, NE)	1.4081 (0.8838, 2.2434) 0.1499	0.1446	
Non-White	196	70 (35.7)	126 (64.3)	14.7 (12.2, NE)	86	27 (31.4)	59 (68.6)	NE (4.4, NE)	0.7297 (0.4629, 1.1501) 0.1746	0.1723	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.5334
Asia	147	47 (32.0)	100 (68.0)	23.3 (12.6, NE)	63	16 (25.4)	47 (74.6)	NE (8.3, NE)	0.7610 (0.4253, 1.3616) 0.3575	0.3566	
North America	58	39 (67.2)	19 (32.8)	3.3 (1.4, 5.4)	28	13 (46.4)	15 (53.6)	4.4 (1.1, NE)	1.2050 (0.6395, 2.2705) 0.5641	0.5490	
Europe + Israel	166	69 (41.6)	97 (58.4)	12.5 (10.3, 20.4)	81	21 (25.9)	60 (74.1)	NE (NE, NE)	1.2175 (0.7409, 2.0007) 0.4375	0.4356	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.0132
0	199	84 (42.2)	115 (57.8)	14.3 (11.0, 24.4)	95	18 (18.9)	77 (81.1)	NE (NE, NE)	1.5577 (0.9295, 2.6104) 0.0925	0.0896	
1	172	71 (41.3)	101 (58.7)	14.7 (10.5, 20.4)	77	32 (41.6)	45 (58.4)	8.3 (3.4, NE)	0.7077 (0.4620, 1.0841) 0.1121	0.1105	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.5084
0	60	21 (35.0)	39 (65.0)	17.1 (12.4, NE)	31	9 (29.0)	22 (71.0)	NE (3.9, NE)	0.8996 (0.4068, 1.9895) 0.7938	0.7946	
1	107	46 (43.0)	61 (57.0)	15.2 (7.4, NE)	48	13 (27.1)	35 (72.9)	NE (NE, NE)	1.3097 (0.7036, 2.4380) 0.3947	0.3928	
2	114	50 (43.9)	64 (56.1)	12.2 (8.2, NE)	50	13 (26.0)	37 (74.0)	NE (NE, NE)	1.1950 (0.6414, 2.2266) 0.5747	0.5737	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	38 (42.2)	52 (57.8)	12.3 (7.5, NE)	43	15 (34.9)	28 (65.1)	8.3 (2.9, NE)	0.6786 (0.3634, 1.2670) 0.2235	0.2199	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.5645
PD	173	68 (39.3)	105 (60.7)	15.0 (10.5, NE)	77	20 (26.0)	57 (74.0)	NE (NE, NE)	1.0355 (0.6224, 1.7228)	0.8913	
PR	48	17 (35.4)	31 (64.6)	13.8 (11.0, NE)	21	7 (33.3)	14 (66.7)	NE (2.9, NE)	0.4742 (0.1804, 1.2462)	0.1194	
SD	82	31 (37.8)	51 (62.2)	23.3 (10.3, NE)	54	15 (27.8)	39 (72.2)	NE (8.3, NE)	1.1104 (0.5942, 2.0750)	0.7426	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.4299
Yes	37	18 (48.6)	19 (51.4)	7.0 (3.4, 24.4)	13	3 (23.1)	10 (76.9)	NE (2.1, NE)	1.5257 (0.4404, 5.2850)	0.5004	
No	334	137 (41.0)	197 (59.0)	14.3 (11.8, 20.4)	159	47 (29.6)	112 (70.4)	NE (8.3, NE)	0.9755 (0.6959, 1.3675)	0.8882	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.9267
Yes	24	9 (37.5)	15 (62.5)	24.4 (3.4, 24.4)	7	2 (28.6)	5 (71.4)	NE (2.1, NE)	1.1406 (0.2384, 5.4562) 0.8691	0.8670	
No	347	146 (42.1)	201 (57.9)	13.8 (11.7, 17.9)	165	48 (29.1)	117 (70.9)	NE (8.3, NE)	1.0148 (0.7281, 1.4145) 0.9308	0.9277	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.8663
Normal Function	201	81 (40.3)	120 (59.7)	15.0 (11.7, 24.4)	80	21 (26.3)	59 (73.8)	NE (8.3, NE)	1.1078 (0.6793, 1.8065) 0.6816	0.6830	
Mild Impairment	123	52 (42.3)	71 (57.7)	13.8 (8.5, NE)	65	19 (29.2)	46 (70.8)	NE (4.4, NE)	0.9607 (0.5609, 1.6453) 0.8839	0.8890	
Moderate Impairment	41	18 (43.9)	23 (56.1)	14.7 (6.9, NE)	23	9 (39.1)	14 (60.9)	NE (1.9, NE)	0.8912 (0.3988, 1.9918) 0.7790	0.7789	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.8074
Normal Function	170	69 (40.6)	101 (59.4)	14.7 (12.2, NE)	88	27 (30.7)	61 (69.3)	NE (8.3, NE)	0.9816 (0.6249, 1.5419) 0.9359	0.9350	
Mild Impairment	194	82 (42.3)	112 (57.7)	12.5 (10.5, 17.1)	82	23 (28.0)	59 (72.0)	NE (4.4, NE)	0.9845 (0.6136, 1.5797) 0.9485	0.9519	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.5123
Yes	331	138 (41.7)	193 (58.3)	13.8 (11.2, 20.4)	146	41 (28.1)	105 (71.9)	NE (NE, NE)	1.0684 (0.7501, 1.5219) 0.7139	0.7111	
No	40	17 (42.5)	23 (57.5)	14.7 (6.6, NE)	26	9 (34.6)	17 (65.4)	NE (2.9, NE)	0.8372 (0.3559, 1.9697) 0.6840	0.6822	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.5175
Positive	329	133 (40.4)	196 (59.6)	15.2 (11.8, 23.3)	152	44 (28.9)	108 (71.1)	NE (NE, NE)	0.9823 (0.6945, 1.3893)	0.9212	
Negative	42	22 (52.4)	20 (47.6)	7.3 (2.8, 14.7)	20	6 (30.0)	14 (70.0)	NE (2.9, NE)	1.2693 (0.4990, 3.2284)	0.6129	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.8873
Positive	331	136 (41.1)	195 (58.9)	15.0 (11.8, 20.4)	155	44 (28.4)	111 (71.6)	NE (NE, NE)	1.0257 (0.7259, 1.4494)	0.8829	
Negative	40	19 (47.5)	21 (52.5)	12.4 (4.0, NE)	17	6 (35.3)	11 (64.7)	4.1 (2.9, NE)	0.9024 (0.3475, 2.3437)	0.8353	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.8481
HER2 IHC 1+	214	22 (10.3)	192 (89.7)	NE (NE, NE)	100	1 (1.0)	99 (99.0)	NE (NE, NE)	5.8839 (0.7846, 44.1237) 0.0847	0.0508	
HER2 IHC 2+/ISH Negative	157	17 (10.8)	140 (89.2)	NE (NE, NE)	72	1 (1.4)	71 (98.6)	NE (NE, NE)	4.5173 (0.5938, 34.3652) 0.1452	0.1109	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.1070
1	220	21 (9.5)	199 (90.5)	NE (NE, NE)	94	2 (2.1)	92 (97.9)	NE (NE, NE)	2.7303 (0.6317, 11.8004) 0.1786	0.1613	
>=2	150	18 (12.0)	132 (88.0)	NE (NE, NE)	78	0	78 (100)	NE (NE, NE)	NE (NE, NE) 0.9922	0.0265	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.2343
Yes	233	25 (10.7)	208 (89.3)	NE (NE, NE)	112	2 (1.8)	110 (98.2)	NE (NE, NE)	3.4769 (0.8116, 14.8954) 0.0932	0.0743	
No	98	10 (10.2)	88 (89.8)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9941	0.1046	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4725
<65	289	32 (11.1)	257 (88.9)	NE (NE, NE)	126	1 (0.8)	125 (99.2)	NE (NE, NE)	7.3681 (0.9983, 54.3824) 0.0502	0.0219	
>=65	82	7 (8.5)	75 (91.5)	NE (NE, NE)	46	1 (2.2)	45 (97.8)	NE (NE, NE)	2.9543 (0.3603, 24.2223) 0.3129	0.2900	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4805
<75	357	37 (10.4)	320 (89.6)	NE (NE, NE)	163	2 (1.2)	161 (98.8)	NE (NE, NE)	4.7361 (1.1299, 19.8516) 0.0334	0.0192	
>=75	14	2 (14.3)	12 (85.7)	NE (5.0, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9979	0.2892	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.1221
White	175	21 (12.0)	154 (88.0)	NE (NE, NE)	85	2 (2.4)	83 (97.6)	NE (NE, NE)	3.1118 (0.7186, 13.4749) 0.1290	0.1099	
Non-White	196	18 (9.2)	178 (90.8)	NE (NE, NE)	86	0	86 (100)	NE (NE, NE)	NE (NE, NE) 0.9925	0.0380	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.4473
Asia	147	12 (8.2)	135 (91.8)	NE (NE, NE)	63	0	63 (100)	NE (NE, NE)	NE (NE, NE) 0.9940	0.1036	
North America	58	9 (15.5)	49 (84.5)	NE (NE, NE)	28	1 (3.6)	27 (96.4)	NE (NE, NE)	2.6668 (0.3322, 21.4056) 0.3560	0.3376	
Europe + Israel	166	18 (10.8)	148 (89.2)	NE (NE, NE)	81	1 (1.2)	80 (98.8)	NE (NE, NE)	5.2075 (0.6849, 39.5949) 0.1109	0.0760	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.7932
0	199	23 (11.6)	176 (88.4)	NE (NE, NE)	95	1 (1.1)	94 (98.9)	NE (NE, NE)	5.9884 (0.8025, 44.6862) 0.0809	0.0474	
1	172	16 (9.3)	156 (90.7)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	4.3358 (0.5652, 33.2633) 0.1582	0.1242	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.6934
0	60	3 (5.0)	57 (95.0)	NE (NE, NE)	31	0	31 (100)	NE (NE, NE)	NE (NE, NE) 0.9966	0.2907	
1	107	8 (7.5)	99 (92.5)	NE (NE, NE)	48	1 (2.1)	47 (97.9)	NE (NE, NE)	2.9970 (0.3739, 24.0244) 0.3014	0.2775	
2	114	19 (16.7)	95 (83.3)	NE (NE, NE)	50	1 (2.0)	49 (98.0)	NE (NE, NE)	4.3519 (0.5725, 33.0832) 0.1553	0.1216	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	9 (10.0)	81 (90.0)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9930	0.2265	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											1.0000
PD	173	20 (11.6)	153 (88.4)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE) 0.9919	0.0223	
PR	48	3 (6.3)	45 (93.8)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	NE (NE, NE) 0.9964	0.5282	
SD	82	7 (8.5)	75 (91.5)	NE (NE, NE)	54	0	54 (100)	NE (NE, NE)	NE (NE, NE) 0.9943	0.0736	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.4882
Yes	37	6 (16.2)	31 (83.8)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9956	0.2250	
No	334	33 (9.9)	301 (90.1)	NE (NE, NE)	159	2 (1.3)	157 (98.7)	NE (NE, NE)	4.3091 (1.0239, 18.1353) 0.0464	0.0301	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.5511
Yes	24	4 (16.7)	20 (83.3)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9964	0.3182	
No	347	35 (10.1)	312 (89.9)	NE (NE, NE)	165	2 (1.2)	163 (98.8)	NE (NE, NE)	4.5708 (1.0891, 19.1840) 0.0378	0.0228	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.3043
Normal Function	201	22 (10.9)	179 (89.1)	NE (NE, NE)	80	1 (1.3)	79 (98.8)	NE (NE, NE)	4.5970 (0.6095, 34.6699) 0.1389	0.1046	
Mild Impairment	123	13 (10.6)	110 (89.4)	NE (NE, NE)	65	0	65 (100)	NE (NE, NE)	NE (NE, NE) 0.9937	0.0760	
Moderate Impairment	41	3 (7.3)	38 (92.7)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	1.4557 (0.1509, 14.0417) 0.7454	0.7439	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.8596
Normal Function	170	15 (8.8)	155 (91.2)	NE (NE, NE)	88	1 (1.1)	87 (98.9)	NE (NE, NE)	4.7367 (0.6169, 36.3685) 0.1348	0.0997	
Mild Impairment	194	24 (12.4)	170 (87.6)	NE (NE, NE)	82	1 (1.2)	81 (98.8)	NE (NE, NE)	5.2973 (0.7086, 39.5997) 0.1043	0.0696	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1699
Yes	331	35 (10.6)	296 (89.4)	NE (NE, NE)	146	1 (0.7)	145 (99.3)	NE (NE, NE)	8.9870 (1.2248, 65.9404) 0.0308	0.0090	
No	40	4 (10.0)	36 (90.0)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	1.7305 (0.1816, 16.4927) 0.6335	0.6272	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.5373
Positive	329	35 (10.6)	294 (89.4)	NE (NE, NE)	152	2 (1.3)	150 (98.7)	NE (NE, NE)	4.7009 (1.1224, 19.6892)	0.0198	
Negative	42	4 (9.5)	38 (90.5)	NE (12.4, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) 0.9967	0.3110	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.5711
Positive	331	35 (10.6)	296 (89.4)	NE (NE, NE)	155	2 (1.3)	153 (98.7)	NE (NE, NE)	4.7649 (1.1374, 19.9607)	0.0186	
Negative	40	4 (10.0)	36 (90.0)	NE (12.4, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) 0.9968	0.3363	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.2310
HER2 IHC 1+	214	23 (10.7)	191 (89.3)	NE (NE, NE)	100	7 (7.0)	93 (93.0)	NE (NE, NE)	1.3035 (0.5552, 3.0602) 0.5427	0.5418	
HER2 IHC 2+/ISH Negative	157	15 (9.6)	142 (90.4)	NE (24.4, NE)	72	9 (12.5)	63 (87.5)	NE (NE, NE)	0.5424 (0.2315, 1.2708) 0.1591	0.1532	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.9508
1	220	21 (9.5)	199 (90.5)	NE (24.4, NE)	94	8 (8.5)	86 (91.5)	NE (NE, NE)	0.9290 (0.4073, 2.1193) 0.8611	0.8622	
>=2	150	17 (11.3)	133 (88.7)	NE (NE, NE)	78	8 (10.3)	70 (89.7)	NE (8.3, NE)	0.8138 (0.3450, 1.9196) 0.6379	0.6375	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.1053
Yes	233	26 (11.2)	207 (88.8)	NE (24.4, NE)	112	9 (8.0)	103 (92.0)	NE (NE, NE)	1.0808 (0.4998, 2.3370) 0.8435	0.8409	
No	98	2 (2.0)	96 (98.0)	NE (NE, NE)	43	3 (7.0)	40 (93.0)	NE (NE, NE)	0.2132 (0.0350, 1.2999) 0.0938	0.0660	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4480
<65	289	30 (10.4)	259 (89.6)	NE (24.4, NE)	126	10 (7.9)	116 (92.1)	NE (NE, NE)	1.0306 (0.4979, 2.1334) 0.9353	0.9368	
>=65	82	8 (9.8)	74 (90.2)	NE (NE, NE)	46	6 (13.0)	40 (87.0)	NE (NE, NE)	0.6315 (0.2158, 1.8480) 0.4015	0.3992	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1289
<75	357	36 (10.1)	321 (89.9)	NE (24.4, NE)	163	16 (9.8)	147 (90.2)	NE (NE, NE)	0.7969 (0.4373, 1.4524) 0.4585	0.4576	
>=75	14	2 (14.3)	12 (85.7)	NE (3.3, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9978	0.2335	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.0818
White	175	25 (14.3)	150 (85.7)	24.4 (24.4, NE)	85	7 (8.2)	78 (91.8)	NE (NE, NE)	1.3744 (0.5884, 3.2108) 0.4625	0.4577	
Non-White	196	13 (6.6)	183 (93.4)	NE (NE, NE)	86	9 (10.5)	77 (89.5)	NE (NE, NE)	0.5015 (0.2106, 1.1941) 0.1190	0.1122	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.1507
Asia	147	5 (3.4)	142 (96.6)	NE (NE, NE)	63	5 (7.9)	58 (92.1)	NE (NE, NE)	0.2871 (0.0775, 1.0639) 0.0619	0.0483	
North America	58	15 (25.9)	43 (74.1)	NE (14.3, NE)	28	4 (14.3)	24 (85.7)	NE (NE, NE)	1.4380 (0.4715, 4.3862) 0.5232	0.5169	
Europe + Israel	166	18 (10.8)	148 (89.2)	24.4 (24.4, NE)	81	7 (8.6)	74 (91.4)	NE (NE, NE)	1.0475 (0.4319, 2.5408) 0.9182	0.9202	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.2504
0	199	16 (8.0)	183 (92.0)	NE (24.4, NE)	95	4 (4.2)	91 (95.8)	NE (NE, NE)	1.4416 (0.4744, 4.3808) 0.5190	0.5162	
1	172	22 (12.8)	150 (87.2)	NE (NE, NE)	77	12 (15.6)	65 (84.4)	NE (8.3, NE)	0.6651 (0.3255, 1.3590) 0.2633	0.2598	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.3560
0	60	7 (11.7)	53 (88.3)	NE (NE, NE)	31	5 (16.1)	26 (83.9)	NE (NE, NE)	0.5717 (0.1796, 1.8201) 0.3440	0.3363	
1	107	11 (10.3)	96 (89.7)	NE (NE, NE)	48	2 (4.2)	46 (95.8)	NE (NE, NE)	2.3466 (0.5197, 10.5956) 0.2674	0.2526	
2	114	12 (10.5)	102 (89.5)	NE (NE, NE)	50	4 (8.0)	46 (92.0)	NE (NE, NE)	0.9548 (0.2978, 3.0608) 0.9380	0.9392	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	8 (8.9)	82 (91.1)	NE (24.4, NE)	43	5 (11.6)	38 (88.4)	NE (8.3, NE)	0.4896 (0.1487, 1.6119) 0.2401	0.2295	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.7449
PD	173	16 (9.2)	157 (90.8)	NE (24.4, NE)	77	7 (9.1)	70 (90.9)	NE (NE, NE)	0.7677 (0.3104, 1.8987)	0.5677	
PR	48	4 (8.3)	44 (91.7)	NE (NE, NE)	21	3 (14.3)	18 (85.7)	NE (NE, NE)	0.3819 (0.0764, 1.9081)	0.2204	
SD	82	5 (6.1)	77 (93.9)	NE (NE, NE)	54	5 (9.3)	49 (90.7)	NE (8.3, NE)	0.4807 (0.1348, 1.7146)	0.2495	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.6778
Yes	37	5 (13.5)	32 (86.5)	24.4 (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	1.0557 (0.1160, 9.6105)	0.9572	
No	334	33 (9.9)	301 (90.1)	NE (NE, NE)	159	15 (9.4)	144 (90.6)	NE (NE, NE)	0.8509 (0.4582, 1.5798)	0.6088	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.1350
Yes	24	4 (16.7)	20 (83.3)	24.4 (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9967	0.3620	
No	347	34 (9.8)	313 (90.2)	NE (NE, NE)	165	16 (9.7)	149 (90.3)	NE (NE, NE)	0.8069 (0.4416, 1.4745) 0.4855	0.4855	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.1510
Normal Function	201	18 (9.0)	183 (91.0)	NE (24.4, NE)	80	6 (7.5)	74 (92.5)	NE (NE, NE)	0.8721 (0.3385, 2.2469) 0.7769	0.7771	
Mild Impairment	123	11 (8.9)	112 (91.1)	NE (NE, NE)	65	9 (13.8)	56 (86.2)	NE (NE, NE)	0.4991 (0.2037, 1.2232) 0.1286	0.1236	
Moderate Impairment	41	6 (14.6)	35 (85.4)	NE (14.7, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	3.2628 (0.3925, 27.1228) 0.2738	0.2469	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.8729
Normal Function	170	16 (9.4)	154 (90.6)	NE (NE, NE)	88	8 (9.1)	80 (90.9)	NE (NE, NE)	0.7390 (0.3107, 1.7578) 0.4938	0.4918	
Mild Impairment	194	18 (9.3)	176 (90.7)	NE (24.4, NE)	82	8 (9.8)	74 (90.2)	NE (NE, NE)	0.7649 (0.3281, 1.7834) 0.5350	0.5390	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.6658
Yes	331	35 (10.6)	296 (89.4)	NE (24.4, NE)	146	15 (10.3)	131 (89.7)	NE (NE, NE)	0.8337 (0.4515, 1.5395) 0.5611	0.5611	
No	40	3 (7.5)	37 (92.5)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	0.9170 (0.0813, 10.3474) 0.9441	0.9441	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.8519
Positive	329	28 (8.5)	301 (91.5)	NE (24.4, NE)	152	12 (7.9)	140 (92.1)	NE (NE, NE)	0.8349 (0.4194, 1.6619)	0.6075	0.6079
Negative	42	10 (23.8)	32 (76.2)	NE (14.7, NE)	20	4 (20.0)	16 (80.0)	NE (3.9, NE)	0.9973 (0.3054, 3.2569)	0.9964	0.9936

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.6182
Positive	331	30 (9.1)	301 (90.9)	NE (24.4, NE)	155	12 (7.7)	143 (92.3)	NE (NE, NE)	0.8987 (0.4544, 1.7775)	0.7598	
Negative	40	8 (20.0)	32 (80.0)	NE (NE, NE)	17	4 (23.5)	13 (76.5)	NE (2.9, NE)	0.7311 (0.2178, 2.4549)	0.6076	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Cough

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.6974
HER2 IHC 1+	214	24 (11.2)	190 (88.8)	NE (NE, NE)	100	10 (10.0)	90 (90.0)	NE (NE, NE)	0.7346 (0.3450, 1.5641) 0.4237	0.4235	
HER2 IHC 2+/ISH Negative	157	12 (7.6)	145 (92.4)	NE (NE, NE)	72	4 (5.6)	68 (94.4)	NE (NE, NE)	1.2067 (0.3849, 3.7834) 0.7472	0.7461	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Cough

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.9584
1	220	19 (8.6)	201 (91.4)	NE (NE, NE)	94	7 (7.4)	87 (92.6)	NE (NE, NE)	0.8557 (0.3549, 2.0628) 0.7285	0.7284	
>=2	150	16 (10.7)	134 (89.3)	NE (NE, NE)	78	7 (9.0)	71 (91.0)	NE (NE, NE)	0.8512 (0.3420, 2.1182) 0.7290	0.7305	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Cough

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.6325
Yes	233	25 (10.7)	208 (89.3)	NE (NE, NE)	112	10 (8.9)	102 (91.1)	NE (NE, NE)	0.9123 (0.4332, 1.9213) 0.8091	0.8100	
No	98	8 (8.2)	90 (91.8)	NE (NE, NE)	43	2 (4.7)	41 (95.3)	NE (NE, NE)	1.1759 (0.2426, 5.6989) 0.8405	0.8403	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Cough

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0990
<65	289	29 (10.0)	260 (90.0)	NE (NE, NE)	126	7 (5.6)	119 (94.4)	NE (NE, NE)	1.2864 (0.5560, 2.9763) 0.5562	0.5551	
>=65	82	7 (8.5)	75 (91.5)	NE (NE, NE)	46	7 (15.2)	39 (84.8)	NE (NE, NE)	0.4681 (0.1627, 1.3465) 0.1591	0.1507	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Cough

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1742
<75	357	36 (10.1)	321 (89.9)	NE (NE, NE)	163	13 (8.0)	150 (92.0)	NE (NE, NE)	0.9096 (0.4764, 1.7366) 0.7739	0.7746	
>=75	14	0	14 (100)	NE (NE, NE)	9	1 (11.1)	8 (88.9)	NE (0.0, NE)	0.0000 (0.0000, ) 0.9984	0.2123	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Cough

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.8202
White	175	16 (9.1)	159 (90.9)	NE (NE, NE)	85	6 (7.1)	79 (92.9)	NE (NE, NE)	1.0231 (0.3961, 2.6421) 0.9624	0.9617	
Non-White	196	20 (10.2)	176 (89.8)	NE (NE, NE)	86	8 (9.3)	78 (90.7)	NE (NE, NE)	0.7643 (0.3308, 1.7656) 0.5292	0.5284	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Cough

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.6896
Asia	147	9 (6.1)	138 (93.9)	NE (NE, NE)	63	4 (6.3)	59 (93.7)	NE (NE, NE)	0.6642 (0.1978, 2.2307) 0.5080	0.5070	
North America	58	11 (19.0)	47 (81.0)	NE (NE, NE)	28	5 (17.9)	23 (82.1)	NE (NE, NE)	0.7394 (0.2483, 2.2015) 0.5876	0.5852	
Europe + Israel	166	16 (9.6)	150 (90.4)	NE (NE, NE)	81	5 (6.2)	76 (93.8)	NE (NE, NE)	1.2432 (0.4518, 3.4205) 0.6734	0.6711	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Cough

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.2311
0	199	14 (7.0)	185 (93.0)	NE (NE, NE)	95	3 (3.2)	92 (96.8)	NE (NE, NE)	1.5889 (0.4501, 5.6087) 0.4718	0.4680	
1	172	22 (12.8)	150 (87.2)	NE (NE, NE)	77	11 (14.3)	66 (85.7)	NE (NE, NE)	0.6573 (0.3124, 1.3831) 0.2690	0.2671	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Cough

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.7532
0	60	4 (6.7)	56 (93.3)	NE (17.1, NE)	31	3 (9.7)	28 (90.3)	NE (NE, NE)	0.4733 (0.1019, 2.1991) 0.3399	0.3296	
1	107	12 (11.2)	95 (88.8)	NE (NE, NE)	48	6 (12.5)	42 (87.5)	NE (NE, NE)	0.8014 (0.3000, 2.1407) 0.6588	0.6582	
2	114	13 (11.4)	101 (88.6)	NE (NE, NE)	50	3 (6.0)	47 (94.0)	NE (NE, NE)	1.2432 (0.3429, 4.5080) 0.7404	0.7392	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Cough

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	7 (7.8)	83 (92.2)	NE (NE, NE)	43	2 (4.7)	41 (95.3)	NE (NE, NE)	1.1823 (0.2386, 5.8580) 0.8375	0.8360	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Cough

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.8191
PD	173	11 (6.4)	162 (93.6)	NE (NE, NE)	77	4 (5.2)	73 (94.8)	NE (NE, NE)	0.8448 (0.2592, 2.7534)	0.7794	
PR	48	5 (10.4)	43 (89.6)	NE (NE, NE)	21	3 (14.3)	18 (85.7)	NE (3.9, NE)	0.7796 (0.1181, 2.1982)	0.3576	
SD	82	6 (7.3)	76 (92.7)	NE (NE, NE)	54	4 (7.4)	50 (92.6)	NE (NE, NE)	0.5096 (0.3661, 0.9088)	0.8827	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Cough

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.8393
Yes	37	4 (10.8)	33 (89.2)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (2.1, NE)	1.3628 (0.1523, 12.1959)	0.7809	
No	334	32 (9.6)	302 (90.4)	NE (NE, NE)	159	13 (8.2)	146 (91.8)	NE (NE, NE)	0.8337 (0.4319, 1.6093)	0.5881	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Cough

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.3746
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	1 (14.3)	6 (85.7)	NE (2.1, NE)	0.3195 (0.0199, 5.1228) 0.4203	0.3952	
No	347	35 (10.1)	312 (89.9)	NE (NE, NE)	165	13 (7.9)	152 (92.1)	NE (NE, NE)	0.9248 (0.4837, 1.7683) 0.8132	0.8141	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Cough

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.3301
Normal Function	201	17 (8.5)	184 (91.5)	NE (NE, NE)	80	7 (8.8)	73 (91.3)	NE (NE, NE)	0.7647 (0.3140, 1.8618) 0.5545	0.5535	
Mild Impairment	123	12 (9.8)	111 (90.2)	NE (NE, NE)	65	2 (3.1)	63 (96.9)	NE (NE, NE)	2.2061 (0.4807, 10.1239) 0.3088	0.2970	
Moderate Impairment	41	6 (14.6)	35 (85.4)	NE (11.0, NE)	23	4 (17.4)	19 (82.6)	NE (NE, NE)	0.6737 (0.1896, 2.3938) 0.5414	0.5389	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Cough

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.8853
Normal Function	170	19 (11.2)	151 (88.8)	NE (NE, NE)	88	8 (9.1)	80 (90.9)	NE (NE, NE)	0.9108 (0.3929, 2.1113) 0.8276	0.8281	
Mild Impairment	194	16 (8.2)	178 (91.8)	NE (NE, NE)	82	6 (7.3)	76 (92.7)	NE (NE, NE)	0.7881 (0.3028, 2.0510) 0.6256	0.6254	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Cough

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.8450
Yes	331	31 (9.4)	300 (90.6)	NE (NE, NE)	146	12 (8.2)	134 (91.8)	NE (NE, NE)	0.8868 (0.4518, 1.7404) 0.7269	0.7277	
No	40	5 (12.5)	35 (87.5)	NE (17.1, NE)	26	2 (7.7)	24 (92.3)	NE (NE, NE)	0.7004 (0.1131, 4.3381) 0.7019	0.7007	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Cough

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.8006
Positive	329	32 (9.7)	297 (90.3)	NE (NE, NE)	152	12 (7.9)	140 (92.1)	NE (NE, NE)	0.9011 (0.4592, 1.7681)	0.7622	
Negative	42	4 (9.5)	38 (90.5)	NE (NE, NE)	20	2 (10.0)	18 (90.0)	NE (3.9, NE)	0.6340 (0.1046, 3.8443)	0.6184	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Cough

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.4562
Positive	331	33 (10.0)	298 (90.0)	NE (NE, NE)	155	12 (7.7)	143 (92.3)	NE (NE, NE)	0.9546 (0.4879, 1.8674)	0.8934	
Negative	40	3 (7.5)	37 (92.5)	NE (NE, NE)	17	2 (11.8)	15 (88.2)	NE (3.9, NE)	0.3415 (0.0465, 2.5058)	0.2692	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											1.0000
HER2 IHC 1+	214	16 (7.5)	198 (92.5)	NE (NE, NE)	100	0	100 (100)	NE (NE, NE)	NE (NE, NE) 0.9926	0.0339	
HER2 IHC 2+/ISH Negative	157	12 (7.6)	145 (92.4)	NE (23.3, NE)	72	0	72 (100)	NE (NE, NE)	NE (NE, NE) 0.9942	0.1049	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											1.0000
1	220	17 (7.7)	203 (92.3)	NE (23.3, NE)	94	0	94 (100)	NE (NE, NE)	NE (NE, NE) 0.9930	0.0495	
>=2	150	11 (7.3)	139 (92.7)	NE (NE, NE)	78	0	78 (100)	NE (NE, NE)	NE (NE, NE) 0.9936	0.0611	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.9995
Yes	233	19 (8.2)	214 (91.8)	NE (20.4, NE)	112	0	112 (100)	NE (NE, NE)	NE (NE, NE) 0.9887	0.0400	
No	98	2 (2.0)	96 (98.0)	NE (23.3, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9979	0.5514	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											1.0000
<65	289	22 (7.6)	267 (92.4)	NE (23.3, NE)	126	0	126 (100)	NE (NE, NE)	NE (NE, NE) 0.9878	0.0274	
>=65	82	6 (7.3)	76 (92.7)	NE (NE, NE)	46	0	46 (100)	NE (NE, NE)	NE (NE, NE) 0.9950	0.1349	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9997
<75	357	28 (7.8)	329 (92.2)	NE (NE, NE)	163	0	163 (100)	NE (NE, NE)	NE (NE, NE) 0.9857	0.0090	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.9996
White	175	18 (10.3)	157 (89.7)	NE (NE, NE)	85	0	85 (100)	NE (NE, NE)	NE (NE, NE) 0.9924	0.0293	
Non-White	196	10 (5.1)	186 (94.9)	NE (23.3, NE)	86	0	86 (100)	NE (NE, NE)	NE (NE, NE) 0.9946	0.1280	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											1.0000
Asia	147	8 (5.4)	139 (94.6)	NE (23.3, NE)	63	0	63 (100)	NE (NE, NE)	NE (NE, NE) 0.9931	0.2269	
North America	58	8 (13.8)	50 (86.2)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9947	0.1261	
Europe + Israel	166	12 (7.2)	154 (92.8)	NE (20.4, NE)	81	0	81 (100)	NE (NE, NE)	NE (NE, NE) 0.9938	0.0706	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.9998
0	199	14 (7.0)	185 (93.0)	NE (23.3, NE)	95	0	95 (100)	NE (NE, NE)	NE (NE, NE) 0.9906	0.0920	
1	172	14 (8.1)	158 (91.9)	NE (20.4, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE) 0.9928	0.0367	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											1.0000
0	60	6 (10.0)	54 (90.0)	NE (NE, NE)	31	0	31 (100)	NE (NE, NE)	NE (NE, NE) 0.9952	0.1698	
1	107	8 (7.5)	99 (92.5)	NE (20.4, NE)	48	0	48 (100)	NE (NE, NE)	NE (NE, NE) 0.9948	0.1216	
2	114	10 (8.8)	104 (91.2)	NE (23.3, NE)	50	0	50 (100)	NE (NE, NE)	NE (NE, NE) 0.9950	0.1520	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	4 (4.4)	86 (95.6)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9954	0.4377	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											NE
PD	173	17 (9.8)	156 (90.2)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE) 0.9922	0.0258	
PR	48	4 (8.3)	44 (91.7)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	NE (NE, NE) 0.9955	0.4319	
SD	82	1 (1.2)	81 (98.8)	NE (23.3, NE)	54	0	54 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											1.0000
Yes	37	3 (8.1)	34 (91.9)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9974	0.4879	
No	334	25 (7.5)	309 (92.5)	NE (NE, NE)	159	0	159 (100)	NE (NE, NE)	NE (NE, NE) 0.9910	0.0097	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.9999
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.5637	
No	347	27 (7.8)	320 (92.2)	NE (NE, NE)	165	0	165 (100)	NE (NE, NE)	NE (NE, NE) 0.9858	0.0091	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											1.0000
Normal Function	201	16 (8.0)	185 (92.0)	NE (23.3, NE)	80	0	80 (100)	NE (NE, NE)	NE (NE, NE) 0.9897	0.0631	
Mild Impairment	123	9 (7.3)	114 (92.7)	NE (NE, NE)	65	0	65 (100)	NE (NE, NE)	NE (NE, NE) 0.9947	0.1344	
Moderate Impairment	41	3 (7.3)	38 (92.7)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9962	0.2447	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.9995
Normal Function	170	7 (4.1)	163 (95.9)	NE (NE, NE)	88	0	88 (100)	NE (NE, NE)	NE (NE, NE) 0.9945	0.1110	
Mild Impairment	194	21 (10.8)	173 (89.2)	NE (20.4, NE)	82	0	82 (100)	NE (NE, NE)	NE (NE, NE) 0.9887	0.0429	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.9997
Yes	331	27 (8.2)	304 (91.8)	NE (23.3, NE)	146	0	146 (100)	NE (NE, NE)	NE (NE, NE) 0.9858	0.0092	
No	40	1 (2.5)	39 (97.5)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9982	0.6225	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.9992
Positive	329	21 (6.4)	308 (93.6)	NE (NE, NE)	152	0	152 (100)	NE (NE, NE)	NE (NE, NE) 0.9880	0.0290	
Negative	42	7 (16.7)	35 (83.3)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) 0.9947	0.1191	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.9991
Positive	331	21 (6.3)	310 (93.7)	NE (NE, NE)	155	0	155 (100)	NE (NE, NE)	NE (NE, NE) 0.9877	0.0235	
Negative	40	7 (17.5)	33 (82.5)	NE (11.1, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) 0.9956	0.2152	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.1783
HER2 IHC 1+	214	14 (6.5)	200 (93.5)	NE (NE, NE)	100	0	100 (100)	NE (NE, NE)	NE (NE, NE) 0.9934	0.0620	
HER2 IHC 2+/ISH Negative	157	9 (5.7)	148 (94.3)	NE (NE, NE)	72	1 (1.4)	71 (98.6)	NE (NE, NE)	2.6180 (0.3268, 20.9692) 0.3646	0.3467	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.2447
1	220	12 (5.5)	208 (94.5)	NE (NE, NE)	94	0	94 (100)	NE (NE, NE)	NE (NE, NE) 0.9938	0.0796	
>=2	150	11 (7.3)	139 (92.7)	NE (NE, NE)	78	1 (1.3)	77 (98.7)	NE (NE, NE)	2.9265 (0.3670, 23.3353) 0.3107	0.2887	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.3306
Yes	233	13 (5.6)	220 (94.4)	NE (NE, NE)	112	1 (0.9)	111 (99.1)	NE (NE, NE)	3.7299 (0.4825, 28.8318) 0.2071	0.1762	
No	98	8 (8.2)	90 (91.8)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9949	0.1400	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2835
<65	289	13 (4.5)	276 (95.5)	NE (NE, NE)	126	0	126 (100)	NE (NE, NE)	NE (NE, NE) 0.9904	0.0849	
>=65	82	10 (12.2)	72 (87.8)	NE (NE, NE)	46	1 (2.2)	45 (97.8)	NE (NE, NE)	3.6878 (0.4654, 29.2197) 0.2165	0.1863	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4479
<75	357	20 (5.6)	337 (94.4)	NE (NE, NE)	163	1 (0.6)	162 (99.4)	NE (NE, NE)	5.1833 (0.6870, 39.1092) 0.1105	0.0755	
>=75	14	3 (21.4)	11 (78.6)	NE (6.9, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9974	0.1803	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.4930
White	175	5 (2.9)	170 (97.1)	NE (NE, NE)	85	0	85 (100)	NE (NE, NE)	NE (NE, NE) 0.9958	0.2322	
Non-White	196	18 (9.2)	178 (90.8)	NE (NE, NE)	86	1 (1.2)	85 (98.8)	NE (NE, NE)	4.6769 (0.6165, 35.4814) 0.1357	0.1009	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.6433
Asia	147	15 (10.2)	132 (89.8)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (NE, NE)	3.9923 (0.5206, 30.6156) 0.1829	0.1505	
North America	58	2 (3.4)	56 (96.6)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9973	0.4390	
Europe + Israel	166	6 (3.6)	160 (96.4)	NE (NE, NE)	81	0	81 (100)	NE (NE, NE)	NE (NE, NE) 0.9957	0.2372	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.2289
0	199	12 (6.0)	187 (94.0)	NE (NE, NE)	95	0	95 (100)	NE (NE, NE)	NE (NE, NE) 0.9934	0.0586	
1	172	11 (6.4)	161 (93.6)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	2.4481 (0.3058, 19.6011) 0.3989	0.3842	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.5254
0	60	3 (5.0)	57 (95.0)	NE (13.8, NE)	31	0	31 (100)	NE (NE, NE)	NE (NE, NE) 0.9975	0.4824	
1	107	6 (5.6)	101 (94.4)	NE (NE, NE)	48	0	48 (100)	NE (NE, NE)	NE (NE, NE) 0.9950	0.1373	
2	114	6 (5.3)	108 (94.7)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	NE (NE, NE) 0.9940	0.2899	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	8 (8.9)	82 (91.1)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	2.0217 (0.2439, 16.7584) 0.5142	0.5060	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.5763
PD	173	7 (4.0)	166 (96.0)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE) 0.9933	0.2268	
PR	48	3 (6.3)	45 (93.8)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	NE (NE, NE) 0.9972	0.6472	
SD	82	8 (9.8)	74 (90.2)	NE (NE, NE)	54	1 (1.9)	53 (98.1)	NE (NE, NE)	4.4562 (0.5536, 35.8703) 0.1602	0.1244	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.9998
Yes	37	0	37 (100)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE)		
No	334	23 (6.9)	311 (93.1)	NE (NE, NE)	159	1 (0.6)	158 (99.4)	NE (NE, NE)	6.3348 (0.8466, 47.3994) 0.0722	0.0396	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.9997
Yes	24	0	24 (100)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE)		
No	347	23 (6.6)	324 (93.4)	NE (NE, NE)	165	1 (0.6)	164 (99.4)	NE (NE, NE)	6.2081 (0.8293, 46.4709) 0.0754	0.0424	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.4412
Normal Function	201	7 (3.5)	194 (96.5)	NE (NE, NE)	80	0	80 (100)	NE (NE, NE)	NE (NE, NE) 0.9928	0.1934	
Mild Impairment	123	10 (8.1)	113 (91.9)	NE (NE, NE)	65	1 (1.5)	64 (98.5)	NE (NE, NE)	2.7312 (0.3383, 22.0476) 0.3457	0.3265	
Moderate Impairment	41	5 (12.2)	36 (87.8)	NE (15.2, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9952	0.1483	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.3097
Normal Function	170	12 (7.1)	158 (92.9)	NE (NE, NE)	88	1 (1.1)	87 (98.9)	NE (NE, NE)	3.7150 (0.4763, 28.9763) 0.2105	0.1799	
Mild Impairment	194	11 (5.7)	183 (94.3)	NE (NE, NE)	82	0	82 (100)	NE (NE, NE)	NE (NE, NE) 0.9943	0.1100	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.0720
Yes	331	19 (5.7)	312 (94.3)	NE (NE, NE)	146	0	146 (100)	NE (NE, NE)	NE (NE, NE) 0.9877	0.0273	
No	40	4 (10.0)	36 (90.0)	NE (18.1, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	1.3019 (0.1218, 13.9115) 0.8272	0.8267	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.6767
Positive	329	21 (6.4)	308 (93.6)	NE (NE, NE)	152	1 (0.7)	151 (99.3)	NE (NE, NE)	5.9009 (0.7862, 44.2875)	0.0503	
Negative	42	2 (4.8)	40 (95.2)	NE (13.8, NE)	20	0	20 (100)	NE (NE, NE)	1.0000 (0.0000, )	1.0000	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.8.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.7033
Positive	331	21 (6.3)	310 (93.7)	NE (NE, NE)	155	1 (0.6)	154 (99.4)	NE (NE, NE)	6.0032 (0.7998, 45.0605)	0.0476	
Negative	40	2 (5.0)	38 (95.0)	NE (13.8, NE)	17	0	17 (100)	NE (NE, NE)	1.0000 (0.0000, )	1.0000	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Rhinorrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.7581
HER2 IHC 1+	214	6 (2.8)	208 (97.2)	NE (NE, NE)	100	1 (1.0)	99 (99.0)	NE (NE, NE)	1.3777 (0.1558, 12.1826) 0.7732	0.7722	
HER2 IHC 2+/ISH Negative	157	8 (5.1)	149 (94.9)	NE (NE, NE)	72	2 (2.8)	70 (97.2)	NE (NE, NE)	1.6021 (0.3375, 7.6048) 0.5531	0.5495	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Rhinorrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.7652
1	220	8 (3.6)	212 (96.4)	NE (NE, NE)	94	2 (2.1)	92 (97.9)	NE (NE, NE)	1.0831 (0.2220, 5.2838) 0.9214	0.9213	
>=2	150	5 (3.3)	145 (96.7)	NE (NE, NE)	78	1 (1.3)	77 (98.7)	NE (NE, NE)	2.0426 (0.2317, 18.0087) 0.5202	0.5115	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Rhinorrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.8425
Yes	233	10 (4.3)	223 (95.7)	NE (NE, NE)	112	2 (1.8)	110 (98.2)	NE (NE, NE)	1.5420 (0.3275, 7.2610) 0.5838	0.5806	
No	98	4 (4.1)	94 (95.9)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	1.5310 (0.1687, 13.8908) 0.7050	0.7027	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Rhinorrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0014
<65	289	13 (4.5)	276 (95.5)	NE (NE, NE)	126	0	126 (100)	NE (NE, NE)	NE (NE, NE) 0.9933	0.0555	
>=65	82	1 (1.2)	81 (98.8)	NE (NE, NE)	46	3 (6.5)	43 (93.5)	NE (NE, NE)	0.1789 (0.0186, 1.7197) 0.1361	0.0927	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Rhinorrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9999
<75	357	14 (3.9)	343 (96.1)	NE (NE, NE)	163	3 (1.8)	160 (98.2)	NE (NE, NE)	1.4722 (0.4132, 5.2457) 0.5508	0.5481	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Rhinorrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.4238
White	175	8 (4.6)	167 (95.4)	NE (NE, NE)	85	1 (1.2)	84 (98.8)	NE (NE, NE)	2.6348 (0.3215, 21.5935) 0.3667	0.3487	
Non-White	196	6 (3.1)	190 (96.9)	NE (NE, NE)	86	2 (2.3)	84 (97.7)	NE (NE, NE)	0.9701 (0.1890, 4.9799) 0.9710	0.9712	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Rhinorrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.6788
Asia	147	2 (1.4)	145 (98.6)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (NE, NE)	0.5830 (0.0480, 7.0816) 0.6719	0.6689	
North America	58	5 (8.6)	53 (91.4)	NE (15.9, NE)	28	1 (3.6)	27 (96.4)	NE (NE, NE)	1.1093 (0.1122, 10.9702) 0.9293	0.9293	
Europe + Israel	166	7 (4.2)	159 (95.8)	NE (NE, NE)	81	1 (1.2)	80 (98.8)	NE (NE, NE)	2.8518 (0.3470, 23.4394) 0.3295	0.3079	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Rhinorrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.0344
0	199	8 (4.0)	191 (96.0)	NE (NE, NE)	95	0	95 (100)	NE (NE, NE)	NE (NE, NE) 0.9941	0.0777	
1	172	6 (3.5)	166 (96.5)	NE (NE, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	0.4741 (0.1074, 2.0935) 0.3247	0.3151	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Rhinorrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.4056
0	60	0	60 (100)	NE (NE, NE)	31	0	31 (100)	NE (NE, NE)	NE (NE, NE)		
1	107	5 (4.7)	102 (95.3)	NE (NE, NE)	48	0	48 (100)	NE (NE, NE)	NE (NE, NE)	0.1656	
2	114	6 (5.3)	108 (94.7)	NE (NE, NE)	50	2 (4.0)	48 (96.0)	NE (NE, NE)	0.9953 0.5982 (0.1078, 3.3178) 0.5566	0.5528	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Rhinorrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	3 (3.3)	87 (96.7)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	1.3632 (0.1417, 13.1144) 0.7885	0.7876	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Rhinorrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.2786
PD	173	5 (2.9)	168 (97.1)	NE (NE, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	1.0440 (0.2023, 5.3870)	0.9586	
PR	48	1 (2.1)	47 (97.9)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	1.0000 (0.0000, )		
SD	82	3 (3.7)	79 (96.3)	NE (NE, NE)	54	0	54 (100)	NE (NE, NE)	NE (NE, NE) 0.9963	0.2617	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Rhinorrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.4087
Yes	37	2 (5.4)	35 (94.6)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9972	0.4218	
No	334	12 (3.6)	322 (96.4)	NE (NE, NE)	159	3 (1.9)	156 (98.1)	NE (NE, NE)	1.2818 (0.3517, 4.6719) 0.7068	0.7061	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Rhinorrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.9999
Yes	24	0	24 (100)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE)		
No	347	14 (4.0)	333 (96.0)	NE (NE, NE)	165	3 (1.8)	162 (98.2)	NE (NE, NE)	1.5567 (0.4378, 5.5350) 0.4941	0.4902	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Rhinorrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0093
Normal Function	201	10 (5.0)	191 (95.0)	NE (NE, NE)	80	0	80 (100)	NE (NE, NE)	NE (NE, NE) 0.9942	0.0942	
Mild Impairment	123	4 (3.3)	119 (96.7)	NE (NE, NE)	65	1 (1.5)	64 (98.5)	NE (NE, NE)	1.2994 (0.1366, 12.3590) 0.8197	0.8192	
Moderate Impairment	41	0	41 (100)	NE (NE, NE)	23	2 (8.7)	21 (91.3)	NE (NE, NE)	0.0000 (0.0000, ) 0.9966	0.0534	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Rhinorrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.9281
Normal Function	170	9 (5.3)	161 (94.7)	NE (NE, NE)	88	2 (2.3)	86 (97.7)	NE (NE, NE)	1.5923 (0.3348, 7.5721) 0.5587	0.5554	
Mild Impairment	194	5 (2.6)	189 (97.4)	NE (NE, NE)	82	1 (1.2)	81 (98.8)	NE (NE, NE)	1.6104 (0.1829, 14.1760) 0.6677	0.6648	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Rhinorrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.9808
Yes	331	10 (3.0)	321 (97.0)	NE (NE, NE)	146	2 (1.4)	144 (98.6)	NE (NE, NE)	1.6604 (0.3580, 7.7014) 0.5172	0.5128	
No	40	4 (10.0)	36 (90.0)	NE (13.0, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	1.4827 (0.1487, 14.7818) 0.7371	0.7355	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Rhinorrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.5119
Positive	329	13 (4.0)	316 (96.0)	NE (NE, NE)	152	3 (2.0)	149 (98.0)	NE (NE, NE)	1.3902 (0.3878, 4.9838)	0.6113	
Negative	42	1 (2.4)	41 (97.6)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) 0.9978	0.4849	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Rhinorrhoea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.9999
Positive	331	14 (4.2)	317 (95.8)	NE (NE, NE)	155	3 (1.9)	152 (98.1)	NE (NE, NE)	1.5575 (0.4392, 5.5237)	0.4888	
Negative	40	0	40 (100)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0169
HER2 IHC 1+	214	71 (33.2)	143 (66.8)	NE (12.0, NE)	100	46 (46.0)	54 (54.0)	4.1 (2.8, NE)	0.4560 (0.3103, 0.6700) 0.0001	<0.0001	
HER2 IHC 2+/ISH Negative	157	75 (47.8)	82 (52.2)	7.2 (4.9, NE)	72	29 (40.3)	43 (59.7)	6.7 (2.3, NE)	0.9512 (0.6164, 1.4678) 0.8212	0.8195	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.7805
1	220	78 (35.5)	142 (64.5)	NE (12.0, NE)	94	38 (40.4)	56 (59.6)	5.8 (3.5, NE)	0.6257 (0.4213, 0.9291) 0.0201	0.0188	
>=2	150	67 (44.7)	83 (55.3)	11.0 (6.4, NE)	78	37 (47.4)	41 (52.6)	3.8 (2.3, NE)	0.6463 (0.4274, 0.9773) 0.0386	0.0370	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.9415
Yes	233	91 (39.1)	142 (60.9)	12.6 (7.2, NE)	112	50 (44.6)	62 (55.4)	4.1 (2.3, 6.9)	0.5796 (0.4056, 0.8283) 0.0028	0.0024	
No	98	34 (34.7)	64 (65.3)	NE (12.0, NE)	43	18 (41.9)	25 (58.1)	NE (2.8, NE)	0.6289 (0.3521, 1.1231) 0.1170	0.1133	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2361
<65	289	114 (39.4)	175 (60.6)	18.1 (11.0, NE)	126	58 (46.0)	68 (54.0)	4.1 (2.3, NE)	0.5686 (0.4105, 0.7876) 0.0007	0.0006	
>=65	82	32 (39.0)	50 (61.0)	NE (7.2, NE)	46	17 (37.0)	29 (63.0)	6.9 (3.8, NE)	0.8401 (0.4627, 1.5250) 0.5667	0.5634	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2267
<75	357	139 (38.9)	218 (61.1)	18.1 (11.0, NE)	163	71 (43.6)	92 (56.4)	4.5 (2.8, NE)	0.6140 (0.4579, 0.8234) 0.0011	0.0010	
>=75	14	7 (50.0)	7 (50.0)	5.5 (0.1, NE)	9	4 (44.4)	5 (55.6)	5.5 (0.7, NE)	1.2455 (0.3625, 4.2792) 0.7274	0.7269	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.3538
White	175	71 (40.6)	104 (59.4)	11.0 (6.5, NE)	85	42 (49.4)	43 (50.6)	4.1 (2.0, 5.8)	0.5681 (0.3837, 0.8411) 0.0047	0.0041	
Non-White	196	75 (38.3)	121 (61.7)	18.1 (11.6, NE)	86	32 (37.2)	54 (62.8)	NE (3.5, NE)	0.7366 (0.4829, 1.1237) 0.1560	0.1538	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.7575
Asia	147	54 (36.7)	93 (63.3)	NE (11.6, NE)	63	23 (36.5)	40 (63.5)	NE (2.8, NE)	0.7424 (0.4517, 1.2202) 0.2401	0.2376	
North America	58	22 (37.9)	36 (62.1)	12.6 (4.9, NE)	28	14 (50.0)	14 (50.0)	4.3 (1.0, NE)	0.5081 (0.2552, 1.0118) 0.0540	0.0497	
Europe + Israel	166	70 (42.2)	96 (57.8)	11.0 (6.9, NE)	81	38 (46.9)	43 (53.1)	4.5 (2.3, 6.9)	0.6113 (0.4067, 0.9186) 0.0179	0.0167	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
ECOG PS											0.9139
0	199	80 (40.2)	119 (59.8)	18.1 (8.3, NE)	95	41 (43.2)	54 (56.8)	4.5 (2.3, NE)	0.6106 (0.4148, 0.8988) 0.0124	0.0113	
1	172	66 (38.4)	106 (61.6)	NE (8.5, NE)	77	34 (44.2)	43 (55.8)	5.0 (2.8, NE)	0.6615 (0.4332, 1.0100) 0.0556	0.0536	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.6428
0	60	27 (45.0)	33 (55.0)	8.3 (3.8, NE)	31	16 (51.6)	15 (48.4)	2.8 (0.7, NE)	0.5822 (0.3085, 1.0985) 0.0949	0.0907	
1	107	35 (32.7)	72 (67.3)	NE (8.5, NE)	48	23 (47.9)	25 (52.1)	5.5 (2.3, NE)	0.5225 (0.3069, 0.8895) 0.0168	0.0149	
2	114	44 (38.6)	70 (61.4)	NE (6.5, NE)	50	21 (42.0)	29 (58.0)	4.3 (2.3, NE)	0.6415 (0.3760, 1.0946) 0.1034	0.0996	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2)											
>=3	90	40 (44.4)	50 (55.6)	11.7 (5.5, NE)	43	15 (34.9)	28 (65.1)	5.8 (2.1, NE)	0.8894 (0.4818, 1.6416) 0.7077	0.7052	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.0753
PD	173	67 (38.7)	106 (61.3)	NE (6.5, NE)	77	34 (44.2)	43 (55.8)	4.5 (3.0, NE)	0.6353 (0.4177, 0.9664)	0.0326	
PR	48	24 (50.0)	24 (50.0)	11.0 (2.9, NE)	21	5 (23.8)	16 (76.2)	NE (2.3, NE)	1.8099 (0.6837, 4.7910)	0.2288	
SD	82	32 (39.0)	50 (61.0)	12.6 (7.2, NE)	54	25 (46.3)	29 (53.7)	5.5 (2.1, NE)	0.5568 (0.3246, 0.9552)	0.0313	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.3249
Yes	37	20 (54.1)	17 (45.9)	5.1 (1.0, 12.4)	13	6 (46.2)	7 (53.8)	6.7 (1.2, 6.7)	0.9275 (0.3613, 2.3809) 0.8757	0.8698	
No	334	126 (37.7)	208 (62.3)	NE (11.0, NE)	159	69 (43.4)	90 (56.6)	5.0 (3.0, NE)	0.6049 (0.4478, 0.8170) 0.0010	0.0009	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.1029
Yes	24	15 (62.5)	9 (37.5)	4.5 (0.8, 12.4)	7	3 (42.9)	4 (57.1)	6.7 (2.1, 6.7)	1.5206 (0.4276, 5.4069) 0.5173	0.5246	
No	347	131 (37.8)	216 (62.2)	NE (11.0, NE)	165	72 (43.6)	93 (56.4)	5.0 (3.0, NE)	0.5983 (0.4456, 0.8033) 0.0006	0.0006	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.1722
Normal Function	201	76 (37.8)	125 (62.2)	NE (10.6, NE)	80	38 (47.5)	42 (52.5)	4.1 (2.3, NE)	0.5601 (0.3758, 0.8349) 0.0044	0.0039	
Mild Impairment	123	58 (47.2)	65 (52.8)	9.4 (5.7, 18.1)	65	24 (36.9)	41 (63.1)	NE (2.7, NE)	0.8833 (0.5415, 1.4409) 0.6193	0.6091	
Moderate Impairment	41	12 (29.3)	29 (70.7)	NE (8.5, NE)	23	11 (47.8)	12 (52.2)	6.7 (3.5, NE)	0.4595 (0.2009, 1.0512) 0.0655	0.0598	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.6836
Normal Function	170	69 (40.6)	101 (59.4)	NE (8.2, NE)	88	42 (47.7)	46 (52.3)	4.5 (2.8, NE)	0.6068 (0.4100, 0.8979) 0.0125	0.0114	
Mild Impairment	194	77 (39.7)	117 (60.3)	12.0 (8.5, NE)	82	33 (40.2)	49 (59.8)	5.8 (2.3, NE)	0.6856 (0.4512, 1.0419) 0.0771	0.0749	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.4755
Yes	331	130 (39.3)	201 (60.7)	12.6 (11.0, NE)	146	63 (43.2)	83 (56.8)	5.0 (3.5, NE)	0.6561 (0.4824, 0.8924) 0.0072	0.0067	
No	40	16 (40.0)	24 (60.0)	NE (5.5, NE)	26	12 (46.2)	14 (53.8)	NE (0.2, NE)	0.5418 (0.2474, 1.1865) 0.1254	0.1196	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.2188
Positive	329	123 (37.4)	206 (62.6)	NE (11.6, NE)	152	66 (43.4)	86 (56.6)	4.5 (2.9, NE)	0.5959 (0.4384, 0.8099) 0.0009	0.0008	
Negative	42	23 (54.8)	19 (45.2)	3.8 (2.5, 12.4)	20	9 (45.0)	11 (55.0)	5.0 (0.2, NE)	0.9381 (0.4292, 2.0503) 0.8728	0.8760	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.2189
Positive	331	125 (37.8)	206 (62.2)	NE (11.6, NE)	155	68 (43.9)	87 (56.1)	4.5 (2.9, NE)	0.5969 (0.4409, 0.8080)	0.0007	
Negative	40	21 (52.5)	19 (47.5)	4.2 (2.5, 12.4)	17	7 (41.2)	10 (58.8)	5.0 (0.3, NE)	0.9885 (0.4145, 2.3576)	0.9788	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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SOC: Nervous system disorders; PT: Headache

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.3413
HER2 IHC 1+	214	22 (10.3)	192 (89.7)	NE (NE, NE)	100	6 (6.0)	94 (94.0)	NE (NE, NE)	1.2885 (0.5138, 3.2311) 0.5890	0.5853	
HER2 IHC 2+/ISH Negative	157	32 (20.4)	125 (79.6)	NE (NE, NE)	72	5 (6.9)	67 (93.1)	NE (11.5, NE)	2.4238 (0.9403, 6.2481) 0.0669	0.0586	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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SOC: Nervous system disorders; PT: Headache

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting									0.4982
1	220	30 (13.6)	190 (86.4) NE (NE, NE)	94	7 (7.4)	87 (92.6) NE (11.5, NE)	1.4240 (0.6208, 3.2663) 0.4040	0.3999	
>=2	150	23 (15.3)	127 (84.7) NE (NE, NE)	78	4 (5.1)	74 (94.9) NE (NE, NE)	2.3357 (0.8001, 6.8188) 0.1207	0.1100	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
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SOC: Nervous system disorders; PT: Headache

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.8768
Yes	233	36 (15.5)	197 (84.5)	NE (NE, NE)	112	8 (7.1)	104 (92.9)	NE (NE, NE)	1.6986 (0.7830, 3.6849) 0.1800	0.1745	
No	98	13 (13.3)	85 (86.7)	NE (NE, NE)	43	3 (7.0)	40 (93.0)	NE (11.5, NE)	1.5927 (0.4518, 5.6151) 0.4691	0.4643	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Nervous system disorders; PT: Headache

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2356
<65	289	49 (17.0)	240 (83.0)	NE (NE, NE)	126	8 (6.3)	118 (93.7)	NE (11.5, NE)	2.0477 (0.9635, 4.3516) 0.0624	0.0571	
>=65	82	5 (6.1)	77 (93.9)	NE (NE, NE)	46	3 (6.5)	43 (93.5)	NE (NE, NE)	0.7609 (0.1786, 3.2406) 0.7116	0.7112	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Headache

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4252
<75	357	53 (14.8)	304 (85.2)	NE (NE, NE)	163	11 (6.7)	152 (93.3)	NE (NE, NE)	1.7047 (0.8846, 3.2852) 0.1110	0.1067	
>=75	14	1 (7.1)	13 (92.9)	NE (5.7, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9985	0.4561	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Headache

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.7177
White	175	31 (17.7)	144 (82.3)	NE (NE, NE)	85	6 (7.1)	79 (92.9)	NE (NE, NE)	2.1204 (0.8801, 5.1082) 0.0939	0.0864	
Non-White	196	23 (11.7)	173 (88.3)	NE (NE, NE)	86	5 (5.8)	81 (94.2)	NE (11.5, NE)	1.4605 (0.5487, 3.8880) 0.4483	0.4446	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Headache

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.4453
Asia	147	15 (10.2)	132 (89.8)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (11.5, NE)	4.1249 (0.5377, 31.6468) 0.1729	0.1397	
North America	58	13 (22.4)	45 (77.6)	NE (10.1, NE)	28	3 (10.7)	25 (89.3)	NE (NE, NE)	1.6464 (0.4643, 5.8388) 0.4401	0.4343	
Europe + Israel	166	26 (15.7)	140 (84.3)	NE (NE, NE)	81	7 (8.6)	74 (91.4)	NE (NE, NE)	1.5728 (0.6798, 3.6388) 0.2900	0.2844	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Headache

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.8217
0	199	36 (18.1)	163 (81.9)	NE (NE, NE)	95	7 (7.4)	88 (92.6)	NE (NE, NE)	1.8506 (0.8178, 4.1875) 0.1396	0.1331	
1	172	18 (10.5)	154 (89.5)	NE (NE, NE)	77	4 (5.2)	73 (94.8)	NE (NE, NE)	1.7218 (0.5775, 5.1338) 0.3296	0.3236	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Headache

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.7052
0	60	10 (16.7)	50 (83.3)	NE (NE, NE)	31	2 (6.5)	29 (93.5)	11.5 (NE, NE)	1.7077 (0.3635, 8.0219) 0.4978	0.4928	
1	107	11 (10.3)	96 (89.7)	NE (NE, NE)	48	4 (8.3)	44 (91.7)	NE (NE, NE)	1.0630 (0.3363, 3.3598) 0.9172	0.9144	
2	114	18 (15.8)	96 (84.2)	NE (NE, NE)	50	2 (4.0)	48 (96.0)	NE (NE, NE)	3.1315 (0.7210, 13.6017) 0.1277	0.1079	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Headache

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 (16.7)	75 (83.3)	NE (NE, NE)	43 (7.0)	40 (93.0)	NE (NE, NE)	1.7929 (0.5120, 6.2780) 0.3612	0.3554	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Headache

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.1428
PD	173	27 (15.6)	146 (84.4)	NE (NE, NE)	77	6 (7.8)	71 (92.2)	NE (NE, NE)	1.6634 (0.6842, 4.0439)	0.2550	
PR	48	10 (20.8)	38 (79.2)	NE (12.4, NE)	21	0	21 (100)	NE (NE, NE)	0.2616 (NE, NE)	0.0744	
SD	82	7 (8.5)	75 (91.5)	NE (NE, NE)	54	3 (5.6)	51 (94.4)	NE (11.5, NE)	0.9811 (0.2474, 3.8905)	0.9784	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Headache

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Reported history of CNS metastases											0.7723
Yes	37	10 (27.0)	27 (73.0)	12.4 (12.4, NE)	13	2 (15.4)	11 (84.6)	NE (2.1, NE)	1.5307 (0.3335, 7.0247) 0.5840	0.5772	
No	334	44 (13.2)	290 (86.8)	NE (NE, NE)	159	9 (5.7)	150 (94.3)	NE (NE, NE)	1.7936 (0.8694, 3.7003) 0.1138	0.1087	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Nervous system disorders; PT: Headache

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.7676
Yes	24	8 (33.3)	16 (66.7)	12.4 (4.5, NE)	7	1 (14.3)	6 (85.7)	NE (2.1, NE)	2.3444 (0.2915, 18.8558) 0.4231	0.4103	
No	347	46 (13.3)	301 (86.7)	NE (NE, NE)	165	10 (6.1)	155 (93.9)	NE (NE, NE)	1.7064 (0.8554, 3.4040) 0.1293	0.1246	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Headache

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.6860
Normal Function	201	33 (16.4)	168 (83.6)	NE (NE, NE)	80	7 (8.8)	73 (91.3)	NE (11.5, NE)	1.5616 (0.6864, 3.5529) 0.2879	0.2843	
Mild Impairment	123	19 (15.4)	104 (84.6)	NE (NE, NE)	65	3 (4.6)	62 (95.4)	NE (NE, NE)	2.2221 (0.6446, 7.6604) 0.2060	0.1938	
Moderate Impairment	41	2 (4.9)	39 (95.1)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	0.8944 (0.0804, 9.9443) 0.9277	0.9276	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Headache

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Hepatic function at baseline											
Normal Function	170	27 (15.9)	143 (84.1)	NE (NE, NE)	88	5 (5.7)	83 (94.3)	NE (NE, NE)	2.3606 (0.9039, 6.1644) 0.0795	0.0706	0.4844
Mild Impairment	194	27 (13.9)	167 (86.1)	NE (NE, NE)	82	6 (7.3)	76 (92.7)	NE (NE, NE)	1.3345 (0.5437, 3.2755) 0.5288	0.5270	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Headache

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.6698
Yes	331	48 (14.5)	283 (85.5)	NE (NE, NE)	146	10 (6.8)	136 (93.2)	NE (NE, NE)	1.6770 (0.8435, 3.3343) 0.1403	0.1356	
No	40	6 (15.0)	34 (85.0)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	2.8854 (0.3441, 24.1922) 0.3287	0.3068	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Nervous system disorders; PT: Headache

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.2104
Positive	329	50 (15.2)	279 (84.8)	NE (NE, NE)	152	11 (7.2)	141 (92.8)	NE (NE, NE)	1.6875 (0.8739, 3.2588) 0.1191	0.1147	
Negative	42	4 (9.5)	38 (90.5)	NE (12.4, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) 0.9969	0.3947	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Headache

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.1868
Positive	331	49 (14.8)	282 (85.2)	NE (NE, NE)	155	11 (7.1)	144 (92.9)	NE (NE, NE)	1.6701 (0.8636, 3.2296)	0.1230	
Negative	40	5 (12.5)	35 (87.5)	NE (12.4, NE)	17	0	17 (100)	NE (NE, NE)	0.1275 (NE, NE) 0.9964	0.3181	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Nervous system disorders; PT: Dysgeusia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.5914
HER2 IHC 1+	214	18 (8.4)	196 (91.6)	NE (NE, NE)	100	9 (9.0)	91 (91.0)	NE (NE, NE)	0.7747 (0.3453, 1.7378) 0.5357	0.5353	
HER2 IHC 2+/ISH Negative	157	19 (12.1)	138 (87.9)	NE (NE, NE)	72	7 (9.7)	65 (90.3)	NE (NE, NE)	0.9298 (0.3860, 2.2394) 0.8710	0.8695	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Nervous system disorders; PT: Dysgeusia

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting									0.5000
1	220	21 (9.5)	199 (90.5)	94	10 (10.6)	84 (89.4)	NE (NE, NE)	0.6891 (0.3206, 1.4813) 0.3402	0.3380
>=2	150	16 (10.7)	134 (89.3)	78	6 (7.7)	72 (92.3)	NE (NE, NE)	1.1100 (0.4297, 2.8671) 0.8293	0.8282

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Nervous system disorders; PT: Dysgeusia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.8494
Yes	233	25 (10.7)	208 (89.3)	NE (NE, NE)	112	12 (10.7)	100 (89.3)	NE (7.9, NE)	0.7245 (0.3592, 1.4614) 0.3681	0.3668	
No	98	5 (5.1)	93 (94.9)	NE (NE, NE)	43	2 (4.7)	41 (95.3)	NE (NE, NE)	0.8507 (0.1623, 4.4590) 0.8483	0.8481	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Nervous system disorders; PT: Dysgeusia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0585
<65	289	24 (8.3)	265 (91.7)	NE (NE, NE)	126	13 (10.3)	113 (89.7)	NE (NE, NE)	0.5671 (0.2846, 1.1301) 0.1069	0.1024	
>=65	82	13 (15.9)	69 (84.1)	NE (NE, NE)	46	3 (6.5)	43 (93.5)	NE (NE, NE)	2.3410 (0.6659, 8.2295) 0.1848	0.1723	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Nervous system disorders; PT: Dysgeusia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3860
<75	357	34 (9.5)	323 (90.5)	NE (NE, NE)	163	15 (9.2)	148 (90.8)	NE (NE, NE)	0.7822 (0.4220, 1.4499) 0.4353	0.4342	
>=75	14	3 (21.4)	11 (78.6)	NE (3.8, NE)	9	1 (11.1)	8 (88.9)	NE (1.0, NE)	2.0578 (0.2134, 19.8407) 0.5325	0.5237	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.9595
White	175	18 (10.3)	157 (89.7)	NE (NE, NE)	85	8 (9.4)	77 (90.6)	NE (NE, NE)	0.8100 (0.3466, 1.8929) 0.6265	0.6256	
Non-White	196	19 (9.7)	177 (90.3)	NE (NE, NE)	86	8 (9.3)	78 (90.7)	NE (NE, NE)	0.8531 (0.3708, 1.9627) 0.7087	0.7094	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Dysgeusia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.3063
Asia	147	15 (10.2)	132 (89.8)	NE (NE, NE)	63	8 (12.7)	55 (87.3)	NE (NE, NE)	0.6421 (0.2701, 1.5266) 0.3161	0.3131	
North America	58	2 (3.4)	56 (96.6)	NE (NE, NE)	28	2 (7.1)	26 (92.9)	7.9 (7.9, NE)	0.2779 (0.0346, 2.2294) 0.2281	0.2017	
Europe + Israel	166	20 (12.0)	146 (88.0)	NE (NE, NE)	81	6 (7.4)	75 (92.6)	NE (NE, NE)	1.2944 (0.5148, 3.2546) 0.5833	0.5822	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Dysgeusia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											
0	199	21 (10.6)	178 (89.4)	NE (NE, NE)	95	10 (10.5)	85 (89.5)	NE (NE, NE)	0.7139 (0.3328, 1.5316) 0.3869	0.3857	0.6468
1	172	16 (9.3)	156 (90.7)	NE (NE, NE)	77	6 (7.8)	71 (92.2)	NE (7.9, NE)	1.0407 (0.4031, 2.6868) 0.9343	0.9353	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Dysgeusia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.9637
0	60	7 (11.7)	53 (88.3)	NE (NE, NE)	31	3 (9.7)	28 (90.3)	NE (NE, NE)	1.1768 (0.3037, 4.5605) 0.8138	0.8155	
1	107	8 (7.5)	99 (92.5)	NE (NE, NE)	48	3 (6.3)	45 (93.8)	NE (NE, NE)	1.0439 (0.2755, 3.9557) 0.9496	0.9491	
2	114	9 (7.9)	105 (92.1)	NE (NE, NE)	50	4 (8.0)	46 (92.0)	NE (NE, NE)	0.6751 (0.2019, 2.2575) 0.5235	0.5212	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Dysgeusia

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 (14.4)	77 (85.6)	NE (NE, NE)	43 (14.0)	37 (86.0)	NE (7.9, NE)	0.6811 (0.2513, 1.8459) 0.4503	0.4474	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Dysgeusia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.7689
PD	173	18 (10.4)	155 (89.6)	NE (NE, NE)	77	6 (7.8)	71 (92.2)	NE (NE, NE)	1.1106 (0.4370, 2.8222)	0.8255	
PR	48	6 (12.5)	42 (87.5)	NE (NE, NE)	21	1 (4.8)	20 (95.2)	NE (NE, NE)	2.3024 (0.2757, 19.2287)	0.4282	
SD	82	10 (12.2)	72 (87.8)	NE (NE, NE)	54	6 (11.1)	48 (88.9)	NE (NE, NE)	0.8724 (0.3136, 2.4269)	0.7926	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Dysgeusia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.0509
Yes	37	6 (16.2)	31 (83.8)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9950	0.1441	
No	334	31 (9.3)	303 (90.7)	NE (NE, NE)	159	16 (10.1)	143 (89.9)	NE (NE, NE)	0.6950 (0.3765, 1.2828) 0.2446	0.2426	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Dysgeusia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0423
Yes	24	6 (25.0)	18 (75.0)	NE (5.5, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9953	0.1784	
No	347	31 (8.9)	316 (91.1)	NE (NE, NE)	165	16 (9.7)	149 (90.3)	NE (NE, NE)	0.6923 (0.3750, 1.2780) 0.2397	0.2379	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Dysgeusia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.1317
Normal Function	201	18 (9.0)	183 (91.0)	NE (NE, NE)	80	8 (10.0)	72 (90.0)	NE (NE, NE)	0.6723 (0.2869, 1.5752) 0.3607	0.3573	
Mild Impairment	123	15 (12.2)	108 (87.8)	NE (NE, NE)	65	7 (10.8)	58 (89.2)	NE (NE, NE)	0.8527 (0.3429, 2.1206) 0.7318	0.7304	
Moderate Impairment	41	4 (9.8)	37 (90.2)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9955	0.1532	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Dysgeusia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.4890
Normal Function	170	20 (11.8)	150 (88.2)	NE (NE, NE)	88	8 (9.1)	80 (90.9)	NE (NE, NE)	1.0264 (0.4480, 2.3516) 0.9509	0.9502	
Mild Impairment	194	17 (8.8)	177 (91.2)	NE (NE, NE)	82	8 (9.8)	74 (90.2)	NE (7.9, NE)	0.6919 (0.2950, 1.6227) 0.3971	0.3947	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Dysgeusia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.7832
Yes	331	34 (10.3)	297 (89.7)	NE (NE, NE)	146	14 (9.6)	132 (90.4)	NE (NE, NE)	0.8503 (0.4532, 1.5953) 0.6135	0.6129	
No	40	3 (7.5)	37 (92.5)	NE (NE, NE)	26	2 (7.7)	24 (92.3)	NE (NE, NE)	0.7593 (0.1227, 4.6995) 0.7672	0.7666	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Dysgeusia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.8790
Positive	329	30 (9.1)	299 (90.9)	NE (NE, NE)	152	13 (8.6)	139 (91.4)	NE (NE, NE)	0.7935 (0.4101, 1.5353) 0.4921	0.4912	
Negative	42	7 (16.7)	35 (83.3)	NE (NE, NE)	20	3 (15.0)	17 (85.0)	NE (NE, NE)	1.0769 (0.2779, 4.1728) 0.9146	0.9144	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Nervous system disorders; PT: Dysgeusia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.5791
Positive	331	30 (9.1)	301 (90.9)	NE (NE, NE)	155	14 (9.0)	141 (91.0)	NE (NE, NE)	0.7507 (0.3944, 1.4289)	0.3813	
Negative	40	7 (17.5)	33 (82.5)	NE (NE, NE)	17	2 (11.8)	15 (88.2)	NE (NE, NE)	1.4726 (0.3047, 7.1173)	0.6322	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Dizziness

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.5293
HER2 IHC 1+	214	14 (6.5)	200 (93.5)	NE (NE, NE)	100	5 (5.0)	95 (95.0)	NE (NE, NE)	0.8611 (0.3033, 2.4449) 0.7789	0.7787	
HER2 IHC 2+/ISH Negative	157	18 (11.5)	139 (88.5)	NE (NE, NE)	72	4 (5.6)	68 (94.4)	NE (NE, NE)	1.6507 (0.5525, 4.9320) 0.3695	0.3651	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Dizziness

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.1195
1	220	20 (9.1)	200 (90.9)	NE (NE, NE)	94	3 (3.2)	91 (96.8)	NE (NE, NE)	2.1632 (0.6366, 7.3505) 0.2163	0.2055	
>=2	150	11 (7.3)	139 (92.7)	NE (NE, NE)	78	6 (7.7)	72 (92.3)	NE (NE, NE)	0.6245 (0.2222, 1.7549) 0.3718	0.3674	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Nervous system disorders; PT: Dizziness

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.4152
Yes	233	21 (9.0)	212 (91.0)	NE (NE, NE)	112	4 (3.6)	108 (96.4)	NE (NE, NE)	1.7896 (0.6049, 5.2947) 0.2930	0.2868	
No	98	8 (8.2)	90 (91.8)	NE (NE, NE)	43	3 (7.0)	40 (93.0)	NE (NE, NE)	0.8935 (0.2324, 3.4358) 0.8699	0.8698	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Nervous system disorders; PT: Dizziness

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9113
<65	289	23 (8.0)	266 (92.0)	NE (NE, NE)	126	6 (4.8)	120 (95.2)	NE (NE, NE)	1.2338 (0.4956, 3.0717) 0.6517	0.6517	
>=65	82	9 (11.0)	73 (89.0)	NE (NE, NE)	46	3 (6.5)	43 (93.5)	NE (NE, NE)	1.2102 (0.3193, 4.5869) 0.7790	0.7812	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Nervous system disorders; PT: Dizziness

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0250
<75	357	32 (9.0)	325 (91.0)	NE (NE, NE)	163	7 (4.3)	156 (95.7)	NE (NE, NE)	1.5351 (0.6697, 3.5188) 0.3112	0.3076	
>=75	14	0	14 (100)	NE (NE, NE)	9	2 (22.2)	7 (77.8)	NE (3.8, NE)	0.0000 (0.0000, ) 0.9979	0.0461	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Nervous system disorders; PT: Dizziness

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.6521
White	175	18 (10.3)	157 (89.7)	NE (NE, NE)	85	6 (7.1)	79 (92.9)	NE (NE, NE)	1.0682 (0.4184, 2.7269) 0.8903	0.8908	
Non-White	196	14 (7.1)	182 (92.9)	NE (NE, NE)	86	3 (3.5)	83 (96.5)	NE (NE, NE)	1.4220 (0.3983, 5.0773) 0.5877	0.5869	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Dizziness

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.8267
Asia	147	12 (8.2)	135 (91.8)	NE (NE, NE)	63	3 (4.8)	60 (95.2)	NE (NE, NE)	1.1782 (0.3227, 4.3020) 0.8040	0.8063	
North America	58	6 (10.3)	52 (89.7)	NE (NE, NE)	28	1 (3.6)	27 (96.4)	NE (NE, NE)	2.0935 (0.2458, 17.8292) 0.4990	0.4896	
Europe + Israel	166	14 (8.4)	152 (91.6)	NE (NE, NE)	81	5 (6.2)	76 (93.8)	NE (NE, NE)	1.0152 (0.3605, 2.8589) 0.9772	0.9782	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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SOC: Nervous system disorders; PT: Dizziness

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.9660
0	199	14 (7.0)	185 (93.0)	NE (NE, NE)	95	4 (4.2)	91 (95.8)	NE (NE, NE)	1.2031 (0.3879, 3.7316) 0.7488	0.7493	
1	172	18 (10.5)	154 (89.5)	NE (NE, NE)	77	5 (6.5)	72 (93.5)	NE (NE, NE)	1.1874 (0.4335, 3.2527) 0.7383	0.7380	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Dizziness

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.7197
0	60	6 (10.0)	54 (90.0)	NE (NE, NE)	31	3 (9.7)	28 (90.3)	NE (5.0, NE)	0.8832 (0.2179, 3.5802) 0.8619	0.8618	
1	107	12 (11.2)	95 (88.8)	NE (NE, NE)	48	2 (4.2)	46 (95.8)	NE (NE, NE)	2.3995 (0.5349, 10.7647) 0.2531	0.2385	
2	114	7 (6.1)	107 (93.9)	NE (NE, NE)	50	2 (4.0)	48 (96.0)	NE (NE, NE)	0.7669 (0.1475, 3.9859) 0.7523	0.7517	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Dizziness

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 (7.8)	83 (92.2)	NE (NE, NE)	43 (4.7)	41 (95.3)	NE (5.6, NE)	1.0514 (0.2098, 5.2695) 0.9514	0.9514	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Dizziness

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.4402
PD	173	13 (7.5)	160 (92.5)	NE (NE, NE)	77	4 (5.2)	73 (94.8)	NE (NE, NE)	1.0954 (0.3507, 3.4213)	0.8758	
PR	48	4 (8.3)	44 (91.7)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	0.8753 (NE, NE)	0.4508	
SD	82	8 (9.8)	74 (90.2)	NE (NE, NE)	54	3 (5.6)	51 (94.4)	NE (NE, NE)	1.3294 (0.3440, 5.1372)	0.6810	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Dizziness

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.1887
Yes	37	4 (10.8)	33 (89.2)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9959	0.2383	
No	334	28 (8.4)	306 (91.6)	NE (NE, NE)	159	9 (5.7)	150 (94.3)	NE (NE, NE)	1.0308 (0.4791, 2.2177) 0.9382	0.9390	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Dizziness

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.9999
Yes	24	0	24 (100)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE)	NE	
No	347	32 (9.2)	315 (90.8)	NE (NE, NE)	165	9 (5.5)	156 (94.5)	NE (NE, NE)	1.2232 (0.5765, 2.5952) 0.5997	0.6000	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Dizziness

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.6556
Normal Function	201	21 (10.4)	180 (89.6)	NE (NE, NE)	80	4 (5.0)	76 (95.0)	NE (NE, NE)	1.5172 (0.5119, 4.4973) 0.4521	0.4490	
Mild Impairment	123	8 (6.5)	115 (93.5)	NE (NE, NE)	65	4 (6.2)	61 (93.8)	NE (NE, NE)	0.6955 (0.2011, 2.4052) 0.5662	0.5632	
Moderate Impairment	41	3 (7.3)	38 (92.7)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	1.5256 (0.1584, 14.6912) 0.7147	0.7126	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Dizziness

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.8613
Normal Function	170	15 (8.8)	155 (91.2)	NE (NE, NE)	88	5 (5.7)	83 (94.3)	NE (NE, NE)	1.0624 (0.3788, 2.9798) 0.9084	0.9084	
Mild Impairment	194	17 (8.8)	177 (91.2)	NE (NE, NE)	82	4 (4.9)	78 (95.1)	NE (NE, NE)	1.3749 (0.4553, 4.1516) 0.5723	0.5717	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Dizziness

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.0760
Yes	331	27 (8.2)	304 (91.8)	NE (NE, NE)	146	9 (6.2)	137 (93.8)	NE (NE, NE)	1.0137 (0.4719, 2.1777) 0.9722	0.9733	
No	40	5 (12.5)	35 (87.5)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9961	0.2256	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Dizziness

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.4981
Positive	329	28 (8.5)	301 (91.5)	NE (NE, NE)	152	7 (4.6)	145 (95.4)	NE (NE, NE)	1.3316 (0.5746, 3.0861) 0.5043	0.5034	
Negative	42	4 (9.5)	38 (90.5)	NE (NE, NE)	20	2 (10.0)	18 (90.0)	NE (5.0, NE)	0.7455 (0.1311, 4.2377) 0.7404	0.7397	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Dizziness

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.2623
Positive	331	29 (8.8)	302 (91.2)	NE (NE, NE)	155	7 (4.5)	148 (95.5)	NE (NE, NE)	1.4179 (0.6138, 3.2755) 0.4137	0.4118	
Negative	40	3 (7.5)	37 (92.5)	NE (NE, NE)	17	2 (11.8)	15 (88.2)	NE (5.0, NE)	0.4124 (0.0631, 2.6934) 0.3549	0.3417	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.6561
HER2 IHC 1+	214	8 (3.7)	206 (96.3)	NE (NE, NE)	100	10 (10.0)	90 (90.0)	NE (NE, NE)	0.2993 (0.1171, 0.7652) 0.0118	0.0076	
HER2 IHC 2+/ISH Negative	157	10 (6.4)	147 (93.6)	NE (NE, NE)	72	9 (12.5)	63 (87.5)	NE (NE, NE)	0.3564 (0.1419, 0.8955) 0.0282	0.0222	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.4485
1	220	9 (4.1)	211 (95.9)	NE (NE, NE)	94	11 (11.7)	83 (88.3)	NE (NE, NE)	0.2591 (0.1060, 0.6334) 0.0031	0.0015	
>=2	150	9 (6.0)	141 (94.0)	NE (NE, NE)	78	8 (10.3)	70 (89.7)	NE (NE, NE)	0.4641 (0.1776, 1.2129) 0.1173	0.1086	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.0959
Yes	233	10 (4.3)	223 (95.7)	NE (NE, NE)	112	15 (13.4)	97 (86.6)	NE (NE, NE)	0.1966 (0.0856, 0.4514) 0.0001	<0.0001	
No	98	7 (7.1)	91 (92.9)	NE (NE, NE)	43	3 (7.0)	40 (93.0)	NE (NE, NE)	0.9624 (0.2487, 3.7250) 0.9558	0.9569	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8265
<65	289	14 (4.8)	275 (95.2)	NE (NE, NE)	126	14 (11.1)	112 (88.9)	NE (NE, NE)	0.2994 (0.1397, 0.6415) 0.0019	0.0010	
>=65	82	4 (4.9)	78 (95.1)	NE (NE, NE)	46	5 (10.9)	41 (89.1)	NE (NE, NE)	0.3895 (0.1043, 1.4550) 0.1608	0.1459	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3486
<75	357	18 (5.0)	339 (95.0)	NE (NE, NE)	163	18 (11.0)	145 (89.0)	NE (NE, NE)	0.3307 (0.1697, 0.6445) 0.0012	0.0007	
>=75	14	0	14 (100)	NE (NE, NE)	9	1 (11.1)	8 (88.9)	NE (0.7, NE)	0.0000 (0.0000, ) 0.9984	0.2294	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.3435
White	175	3 (1.7)	172 (98.3)	NE (NE, NE)	85	6 (7.1)	79 (92.9)	NE (NE, NE)	0.1734 (0.0423, 0.7102) 0.0149	0.0063	
Non-White	196	15 (7.7)	181 (92.3)	NE (NE, NE)	86	13 (15.1)	73 (84.9)	NE (NE, NE)	0.3873 (0.1824, 0.8224) 0.0136	0.0105	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.4992
Asia	147	14 (9.5)	133 (90.5)	NE (NE, NE)	63	11 (17.5)	52 (82.5)	NE (NE, NE)	0.4121 (0.1850, 0.9181) 0.0301	0.0251	
North America	58	3 (5.2)	55 (94.8)	NE (14.1, NE)	28	5 (17.9)	23 (82.1)	NE (4.3, NE)	0.1375 (0.0265, 0.7132) 0.0182	0.0058	
Europe + Israel	166	1 (0.6)	165 (99.4)	NE (NE, NE)	81	3 (3.7)	78 (96.3)	NE (NE, NE)	0.1409 (0.0146, 1.3608) 0.0903	0.0484	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.3695
0	199	10 (5.0)	189 (95.0)	NE (NE, NE)	95	13 (13.7)	82 (86.3)	NE (NE, NE)	0.2532 (0.1091, 0.5875) 0.0014	0.0006	
1	172	8 (4.7)	164 (95.3)	NE (NE, NE)	77	6 (7.8)	71 (92.2)	NE (NE, NE)	0.4963 (0.1704, 1.4455) 0.1990	0.1900	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.2043
0	60	1 (1.7)	59 (98.3)	NE (NE, NE)	31	3 (9.7)	28 (90.3)	NE (NE, NE)	0.1517 (0.0157, 1.4653) 0.1031	0.0603	
1	107	3 (2.8)	104 (97.2)	NE (NE, NE)	48	5 (10.4)	43 (89.6)	NE (NE, NE)	0.2253 (0.0535, 0.9477) 0.0420	0.0262	
2	114	11 (9.6)	103 (90.4)	NE (NE, NE)	50	5 (10.0)	45 (90.0)	NE (NE, NE)	0.6808 (0.2297, 2.0177) 0.4880	0.4850	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	3 (3.3)	87 (96.7)	NE (NE, NE)	43	6 (14.0)	37 (86.0)	NE (NE, NE)	0.1862 (0.0457, 0.7591) 0.0191	0.0090	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.5327
PD	173	9 (5.2)	164 (94.8)	NE (NE, NE)	77	5 (6.5)	72 (93.5)	NE (NE, NE)	0.5002 (0.1632, 1.5334)	0.2170	
PR	48	3 (6.3)	45 (93.8)	NE (NE, NE)	21	3 (14.3)	18 (85.7)	NE (NE, NE)	0.2255 (0.0697, 1.7327)	0.1774	
SD	82	5 (6.1)	77 (93.9)	NE (NE, NE)	54	9 (16.7)	45 (83.3)	NE (NE, NE)	0.3476 (0.1028, 0.9338)	0.0279	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.7838
Yes	37	2 (5.4)	35 (94.6)	NE (NE, NE)	13	2 (15.4)	11 (84.6)	NE (2.3, NE)	0.2224 (0.0289, 1.7119)	0.1170	
No	334	16 (4.8)	318 (95.2)	NE (NE, NE)	159	17 (10.7)	142 (89.3)	NE (NE, NE)	0.3341 (0.1666, 0.6698)	0.0012	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.8723
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	1 (14.3)	6 (85.7)	NE (2.3, NE)	0.3100 (0.0194, 4.9570) 0.4076	0.3809	
No	347	17 (4.9)	330 (95.1)	NE (NE, NE)	165	18 (10.9)	147 (89.1)	NE (NE, NE)	0.3278 (0.1667, 0.6443) 0.0012	0.0007	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.4266
Normal Function	201	6 (3.0)	195 (97.0)	NE (NE, NE)	80	7 (8.8)	73 (91.3)	NE (NE, NE)	0.2011 (0.0624, 0.6476) 0.0072	0.0030	
Mild Impairment	123	11 (8.9)	112 (91.1)	NE (NE, NE)	65	8 (12.3)	57 (87.7)	NE (NE, NE)	0.5471 (0.2165, 1.3825) 0.2022	0.1960	
Moderate Impairment	41	1 (2.4)	40 (97.6)	NE (NE, NE)	23	3 (13.0)	20 (87.0)	NE (NE, NE)	0.1694 (0.0176, 1.6307) 0.1244	0.0809	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.0631
Normal Function	170	7 (4.1)	163 (95.9)	NE (NE, NE)	88	14 (15.9)	74 (84.1)	NE (NE, NE)	0.2069 (0.0830, 0.5158) 0.0007	0.0002	
Mild Impairment	194	11 (5.7)	183 (94.3)	NE (NE, NE)	82	5 (6.1)	77 (93.9)	NE (NE, NE)	0.6452 (0.2189, 1.9019) 0.4269	0.4242	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.2920
Yes	331	16 (4.8)	315 (95.2)	NE (NE, NE)	146	14 (9.6)	132 (90.4)	NE (NE, NE)	0.3749 (0.1809, 0.7770) 0.0083	0.0061	
No	40	2 (5.0)	38 (95.0)	NE (NE, NE)	26	5 (19.2)	21 (80.8)	NE (NE, NE)	0.2066 (0.0394, 1.0839) 0.0622	0.0403	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.9266
Positive	329	17 (5.2)	312 (94.8)	NE (NE, NE)	152	18 (11.8)	134 (88.2)	NE (NE, NE)	0.3224 (0.1643, 0.6327)	0.0005	
Negative	42	1 (2.4)	41 (97.6)	NE (NE, NE)	20	1 (5.0)	19 (95.0)	NE (NE, NE)	0.3986 (0.0247, 6.4426)	0.5024	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Peripheral sensory neuropathy

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.9708
Positive	331	17 (5.1)	314 (94.9)	NE (NE, NE)	155	18 (11.6)	137 (88.4)	NE (NE, NE)	0.3245 (0.1654, 0.6367)	0.0006	
Negative	40	1 (2.5)	39 (97.5)	NE (NE, NE)	17	1 (5.9)	16 (94.1)	NE (NE, NE)	0.4177 (0.0261, 6.6782)	0.5239	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Neuropathy peripheral

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.8321
HER2 IHC 1+	214	6 (2.8)	208 (97.2)	NE (NE, NE)	100	8 (8.0)	92 (92.0)	NE (NE, NE)	0.1853 (0.0610, 0.5631) 0.0030	0.0010	
HER2 IHC 2+/ISH Negative	157	7 (4.5)	150 (95.5)	NE (NE, NE)	72	8 (11.1)	64 (88.9)	NE (NE, NE)	0.2807 (0.0990, 0.7962) 0.0169	0.0111	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Neuropathy peripheral

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.5036
1	220	6 (2.7)	214 (97.3)	NE (NE, NE)	94	9 (9.6)	85 (90.4)	NE (NE, NE)	0.1867 (0.0647, 0.5390) 0.0019	0.0006	
>=2	150	7 (4.7)	143 (95.3)	NE (NE, NE)	78	7 (9.0)	71 (91.0)	NE (7.4, NE)	0.3084 (0.1029, 0.9237) 0.0356	0.0272	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Neuropathy peripheral

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.3498
Yes	233	10 (4.3)	223 (95.7)	NE (NE, NE)	112	11 (9.8)	101 (90.2)	NE (7.4, NE)	0.2427 (0.0989, 0.5958) 0.0020	0.0009	
No	98	2 (2.0)	96 (98.0)	NE (NE, NE)	43	5 (11.6)	38 (88.4)	NE (NE, NE)	0.1282 (0.0243, 0.6757) 0.0154	0.0046	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Neuropathy peripheral

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2016
<65	289	9 (3.1)	280 (96.9)	NE (NE, NE)	126	13 (10.3)	113 (89.7)	NE (NE, NE)	0.1867 (0.0772, 0.4519) 0.0002	<0.0001	
>=65	82	4 (4.9)	78 (95.1)	NE (NE, NE)	46	3 (6.5)	43 (93.5)	NE (NE, NE)	0.4727 (0.1029, 2.1715) 0.3355	0.3251	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Neuropathy peripheral

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5231
<75	357	12 (3.4)	345 (96.6)	NE (NE, NE)	163	15 (9.2)	148 (90.8)	NE (NE, NE)	0.2250 (0.1021, 0.4958) 0.0002	<0.0001	
>=75	14	1 (7.1)	13 (92.9)	NE (5.5, NE)	9	1 (11.1)	8 (88.9)	NE (5.5, NE)	0.4473 (0.0279, 7.1816) 0.5700	0.5596	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Neuropathy peripheral

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.4050
White	175	7 (4.0)	168 (96.0)	NE (NE, NE)	85	11 (12.9)	74 (87.1)	NE (7.4, NE)	0.1781 (0.0664, 0.4778) 0.0006	0.0001	
Non-White	196	6 (3.1)	190 (96.9)	NE (NE, NE)	86	5 (5.8)	81 (94.2)	NE (NE, NE)	0.3463 (0.1013, 1.1839) 0.0909	0.0779	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Neuropathy peripheral

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.7765
Asia	147	3 (2.0)	144 (98.0)	NE (NE, NE)	63	2 (3.2)	61 (96.8)	NE (NE, NE)	0.6173 (0.1030, 3.6977) 0.5974	0.5939	
North America	58	2 (3.4)	56 (96.6)	NE (NE, NE)	28	3 (10.7)	25 (89.3)	NE (5.8, NE)	0.1783 (0.0292, 1.0891) 0.0618	0.0361	
Europe + Israel	166	8 (4.8)	158 (95.2)	NE (NE, NE)	81	11 (13.6)	70 (86.4)	NE (7.4, NE)	0.1921 (0.0736, 0.5018) 0.0008	0.0002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Neuropathy peripheral

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.5377
0	199	5 (2.5)	194 (97.5)	NE (NE, NE)	95	8 (8.4)	87 (91.6)	NE (NE, NE)	0.1967 (0.0633, 0.6108) 0.0049	0.0019	
1	172	8 (4.7)	164 (95.3)	NE (NE, NE)	77	8 (10.4)	69 (89.6)	NE (7.4, NE)	0.2282 (0.0769, 0.6775) 0.0078	0.0040	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Neuropathy peripheral

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.6525
0	60	1 (1.7)	59 (98.3)	NE (NE, NE)	31	3 (9.7)	28 (90.3)	NE (NE, NE)	0.1629 (0.0169, 1.5666)	0.0726	
1	107	2 (1.9)	105 (98.1)	NE (NE, NE)	48	5 (10.4)	43 (89.6)	NE (NE, NE)	0.1155 (0.0220, 0.6072)	0.0024	
2	114	6 (5.3)	108 (94.7)	NE (NE, NE)	50	4 (8.0)	46 (92.0)	NE (NE, NE)	0.3869 (0.1026, 1.4581)	0.1472	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Neuropathy peripheral

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	4 (4.4)	86 (95.6)	NE (NE, NE)	43	4 (9.3)	39 (90.7)	NE (5.8, NE)	0.3052 (0.0723, 1.2876) 0.1061	0.0889	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Neuropathy peripheral

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.9957
PD	173	6 (3.5)	167 (96.5)	NE (NE, NE)	77	7 (9.1)	70 (90.9)	NE (NE, NE)	0.2050 (0.0649, 0.6476)	0.0031	
PR	48	1 (2.1)	47 (97.9)	NE (NE, NE)	21	1 (4.8)	20 (95.2)	NE (NE, NE)	0.3536 (0.0218, 5.7421)	0.4452	
SD	82	3 (3.7)	79 (96.3)	NE (NE, NE)	54	6 (11.1)	48 (88.9)	NE (7.4, NE)	0.2084 (0.0494, 0.8789)	0.0203	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Neuropathy peripheral

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.0648
Yes	37	0	37 (100)	NE (NE, NE)	13	2 (15.4)	11 (84.6)	7.4 (2.1, NE)	0.0000 (0.0000, ) 0.9978	0.0010	
No	334	13 (3.9)	321 (96.1)	NE (NE, NE)	159	14 (8.8)	145 (91.2)	NE (NE, NE)	0.2864 (0.1315, 0.6236) 0.0016	0.0008	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Neuropathy peripheral

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0667
Yes	24	0	24 (100)	NE (NE, NE)	7	2 (28.6)	5 (71.4)	7.4 (2.1, NE)	0.0000 (0.0000, ) 0.9981	0.0033	
No	347	13 (3.7)	334 (96.3)	NE (NE, NE)	165	14 (8.5)	151 (91.5)	NE (NE, NE)	0.2815 (0.1292, 0.6134) 0.0014	0.0007	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Neuropathy peripheral

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.8646
Normal Function	201	7 (3.5)	194 (96.5)	NE (NE, NE)	80	8 (10.0)	72 (90.0)	NE (NE, NE)	0.2192 (0.0761, 0.6310) 0.0049	0.0022	
Mild Impairment	123	4 (3.3)	119 (96.7)	NE (NE, NE)	65	4 (6.2)	61 (93.8)	NE (NE, NE)	0.3946 (0.0974, 1.5992) 0.1928	0.1788	
Moderate Impairment	41	2 (4.9)	39 (95.1)	NE (NE, NE)	23	3 (13.0)	20 (87.0)	NE (6.9, NE)	0.2382 (0.0393, 1.4436) 0.1186	0.0906	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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SOC: Nervous system disorders; PT: Neuropathy peripheral

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.6780
Normal Function	170	5 (2.9)	165 (97.1)	NE (NE, NE)	88	6 (6.8)	82 (93.2)	NE (NE, NE)	0.2448 (0.0705, 0.8501) 0.0267	0.0178	
Mild Impairment	194	8 (4.1)	186 (95.9)	NE (NE, NE)	82	10 (12.2)	72 (87.8)	NE (6.9, NE)	0.2047 (0.0785, 0.5342) 0.0012	0.0004	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Neuropathy peripheral

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1277
Yes	331	13 (3.9)	318 (96.1)	NE (NE, NE)	146	14 (9.6)	132 (90.4)	NE (NE, NE)	0.2564 (0.1177, 0.5583) 0.0006	0.0002	
No	40	0	40 (100)	NE (NE, NE)	26	2 (7.7)	24 (92.3)	NE (NE, NE)	0.0000 (0.0000, ) 0.9965	0.0765	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Nervous system disorders; PT: Neuropathy peripheral

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.8459
Positive	329	12 (3.6)	317 (96.4)	NE (NE, NE)	152	15 (9.9)	137 (90.1)	NE (NE, NE)	0.2225 (0.1016, 0.4873) 0.0002	<0.0001	
Negative	42	1 (2.4)	41 (97.6)	NE (NE, NE)	20	1 (5.0)	19 (95.0)	NE (NE, NE)	0.4698 (0.0294, 7.5113) 0.5932	0.5844	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Neuropathy peripheral

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.2117
Positive	331	12 (3.6)	319 (96.4)	NE (NE, NE)	155	16 (10.3)	139 (89.7)	NE (NE, NE)	0.2141 (0.0988, 0.4640)	0.0001	<0.0001
Negative	40	1 (2.5)	39 (97.5)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) 0.9978		0.5091

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.5377
HER2 IHC 1+	214	76 (35.5)	138 (64.5)	19.6 (12.1, NE)	100	29 (29.0)	71 (71.0)	11.8 (6.8, NE)	0.8068 (0.5198, 1.2523) 0.3386	0.3395	
HER2 IHC 2+/ISH Negative	157	60 (38.2)	97 (61.8)	16.5 (9.0, NE)	72	27 (37.5)	45 (62.5)	6.9 (4.0, NE)	0.6434 (0.4020, 1.0297) 0.0660	0.0634	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.1836
1	220	82 (37.3)	138 (62.7)	19.6 (9.0, NE)	94	37 (39.4)	57 (60.6)	6.1 (3.7, NE)	0.6157 (0.4134, 0.9170) 0.0170	0.0160	
>=2	150	53 (35.3)	97 (64.7)	16.5 (11.7, NE)	78	19 (24.4)	59 (75.6)	11.8 (6.8, NE)	0.9239 (0.5367, 1.5903) 0.7752	0.7734	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.9272
Yes	233	89 (38.2)	144 (61.8)	12.9 (9.0, NE)	112	38 (33.9)	74 (66.1)	11.0 (6.0, NE)	0.7167 (0.4838, 1.0618) 0.0967	0.0946	
No	98	40 (40.8)	58 (59.2)	22.7 (9.0, NE)	43	17 (39.5)	26 (60.5)	6.8 (3.8, NE)	0.7022 (0.3935, 1.2529) 0.2314	0.2293	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8942
<65	289	109 (37.7)	180 (62.3)	13.5 (11.7, NE)	126	41 (32.5)	85 (67.5)	11.0 (6.1, NE)	0.7198 (0.4963, 1.0440) 0.0831	0.0818	
>=65	82	27 (32.9)	55 (67.1)	NE (7.8, NE)	46	15 (32.6)	31 (67.4)	NE (4.0, NE)	0.7737 (0.4088, 1.4644) 0.4306	0.4276	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3081
<75	357	131 (36.7)	226 (63.3)	16.5 (12.1, NE)	163	54 (33.1)	109 (66.9)	11.0 (6.1, NE)	0.6990 (0.5037, 0.9700) 0.0322	0.0314	
>=75	14	5 (35.7)	9 (64.3)	NE (2.1, NE)	9	2 (22.2)	7 (77.8)	NE (3.7, NE)	1.4453 (0.2753, 7.5889) 0.6633	0.6616	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.8106
White	175	76 (43.4)	99 (56.6)	12.1 (7.0, NE)	85	31 (36.5)	54 (63.5)	6.9 (3.8, 11.0)	0.7579 (0.4917, 1.1681) 0.2092	0.2076	
Non-White	196	60 (30.6)	136 (69.4)	19.6 (12.5, NE)	86	25 (29.1)	61 (70.9)	11.8 (6.8, NE)	0.6939 (0.4299, 1.1199) 0.1345	0.1328	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.7152
Asia	147	39 (26.5)	108 (73.5)	NE (19.6, NE)	63	12 (19.0)	51 (81.0)	NE (NE, NE)	0.9932 (0.5139, 1.9194) 0.9837	0.9831	
North America	58	27 (46.6)	31 (53.4)	9.0 (4.9, 16.5)	28	12 (42.9)	16 (57.1)	6.0 (2.1, NE)	0.6294 (0.3059, 1.2949) 0.2084	0.2064	
Europe + Israel	166	70 (42.2)	96 (57.8)	10.8 (7.6, NE)	81	32 (39.5)	49 (60.5)	6.9 (3.8, 11.8)	0.6551 (0.4247, 1.0104) 0.0557	0.0542	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.7795
0	199	75 (37.7)	124 (62.3)	16.5 (10.5, NE)	95	29 (30.5)	66 (69.5)	11.0 (6.8, NE)	0.7677 (0.4946, 1.1915) 0.2385	0.2390	
1	172	61 (35.5)	111 (64.5)	12.6 (10.0, NE)	77	27 (35.1)	50 (64.9)	6.9 (4.0, 11.8)	0.6791 (0.4240, 1.0875) 0.1072	0.1044	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1605
0	60	15 (25.0)	45 (75.0)	NE (10.8, NE)	31	5 (16.1)	26 (83.9)	NE (NE, NE)	1.1377 (0.4051, 3.1951) 0.8066	0.8070	
1	107	35 (32.7)	72 (67.3)	19.6 (9.0, NE)	48	22 (45.8)	26 (54.2)	6.9 (2.3, NE)	0.4845 (0.2808, 0.8361) 0.0092	0.0079	
2	114	49 (43.0)	65 (57.0)	12.5 (7.8, NE)	50	20 (40.0)	30 (60.0)	6.8 (2.7, 11.8)	0.6531 (0.3798, 1.1229) 0.1234	0.1199	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	37 (41.1)	53 (58.9)	12.1 (7.1, NE)	43	9 (20.9)	34 (79.1)	NE (3.7, NE)	1.2260 (0.5801, 2.5911) 0.5936	0.5922	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.3386
PD	173	62 (35.8)	111 (64.2)	22.7 (9.0, NE)	77	21 (27.3)	56 (72.7)	11.8 (6.0, 11.8)	0.8530 (0.5137, 1.4165)	0.5379	
PR	48	17 (35.4)	31 (64.6)	19.6 (10.0, 19.6)	21	6 (28.6)	15 (71.4)	NE (6.8, NE)	0.5390 (0.3289, 2.2162)	0.7529	
SD	82	23 (28.0)	59 (72.0)	NE (12.9, NE)	54	19 (35.2)	35 (64.8)	6.9 (3.7, NE)	0.5140 (0.2734, 0.9662)	0.0359	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.4176
Yes	37	15 (40.5)	22 (59.5)	12.1 (3.7, NE)	13	3 (23.1)	10 (76.9)	6.9 (1.4, NE)	1.2030 (0.3385, 4.2755) 0.7751	0.7743	
No	334	121 (36.2)	213 (63.8)	19.6 (12.4, NE)	159	53 (33.3)	106 (66.7)	11.0 (6.1, NE)	0.7028 (0.5039, 0.9801) 0.0376	0.0369	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.9084
Yes	24	7 (29.2)	17 (70.8)	NE (3.0, NE)	7	2 (28.6)	5 (71.4)	6.9 (0.3, NE)	0.9041 (0.1857, 4.4019) 0.9006	0.8951	
No	347	129 (37.2)	218 (62.8)	16.5 (11.7, NE)	165	54 (32.7)	111 (67.3)	11.0 (6.1, NE)	0.7220 (0.5203, 1.0019) 0.0514	0.0506	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.8.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.3407
Normal Function	201	71 (35.3)	130 (64.7)	19.6 (12.5, NE)	80	27 (33.8)	53 (66.3)	NE (6.0, NE)	0.6975 (0.4427, 1.0992) 0.1206	0.1207	
Mild Impairment	123	45 (36.6)	78 (63.4)	12.4 (9.0, NE)	65	21 (32.3)	44 (67.7)	11.0 (6.8, 11.8)	0.6332 (0.3681, 1.0892) 0.0987	0.0954	
Moderate Impairment	41	19 (46.3)	22 (53.7)	8.0 (4.9, NE)	23	7 (30.4)	16 (69.6)	6.9 (3.7, NE)	1.2876 (0.5348, 3.1000) 0.5728	0.5734	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1836
Normal Function	170	69 (40.6)	101 (59.4)	13.5 (10.0, NE)	88	27 (30.7)	61 (69.3)	NE (6.0, NE)	0.8703 (0.5513, 1.3738) 0.5508	0.5491	
Mild Impairment	194	65 (33.5)	129 (66.5)	NE (10.5, NE)	82	29 (35.4)	53 (64.6)	11.0 (3.7, 11.8)	0.5913 (0.3755, 0.9309) 0.0233	0.0218	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.0423
Yes	331	118 (35.6)	213 (64.4)	19.6 (12.1, NE)	146	52 (35.6)	94 (64.4)	11.0 (6.0, NE)	0.6412 (0.4580, 0.8978) 0.0097	0.0092	
No	40	18 (45.0)	22 (55.0)	12.4 (4.9, NE)	26	4 (15.4)	22 (84.6)	NE (NE, NE)	2.0751 (0.6869, 6.2690) 0.1956	0.1863	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.6198
Positive	329	127 (38.6)	202 (61.4)	13.5 (11.7, NE)	152	53 (34.9)	99 (65.1)	11.0 (6.0, NE)	0.7127 (0.5124, 0.9911)	0.0433	
Negative	42	9 (21.4)	33 (78.6)	NE (10.8, NE)	20	3 (15.0)	17 (85.0)	NE (NE, NE)	1.0086 (0.2576, 3.9494)	0.9902	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.4001
Positive	331	130 (39.3)	201 (60.7)	13.5 (10.5, NE)	155	55 (35.5)	100 (64.5)	11.0 (6.0, NE)	0.7240 (0.5235, 1.0013)	0.0499	
Negative	40	6 (15.0)	34 (85.0)	NE (10.8, NE)	17	1 (5.9)	16 (94.1)	NE (NE, NE)	1.3221 (0.1439, 12.1501)	0.8045	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.9434
HER2 IHC 1+	214	26 (12.1)	188 (87.9)	NE (22.7, NE)	100	12 (12.0)	88 (88.0)	NE (9.6, NE)	0.5438 (0.2656, 1.1133) 0.0957	0.0910	
HER2 IHC 2+/ISH Negative	157	17 (10.8)	140 (89.2)	NE (NE, NE)	72	8 (11.1)	64 (88.9)	NE (11.5, NE)	0.5184 (0.2152, 1.2488) 0.1430	0.1369	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.3371
1	220	26 (11.8)	194 (88.2)	NE (22.7, NE)	94	14 (14.9)	80 (85.1)	NE (11.5, NE)	0.4762 (0.2424, 0.9355) 0.0313	0.0278	
>=2	150	16 (10.7)	134 (89.3)	NE (NE, NE)	78	6 (7.7)	72 (92.3)	NE (9.6, NE)	0.6450 (0.2403, 1.7308) 0.3839	0.3803	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.5246
Yes	233	26 (11.2)	207 (88.8)	NE (NE, NE)	112	14 (12.5)	98 (87.5)	NE (11.5, NE)	0.4995 (0.2529, 0.9867) 0.0457	0.0418	
No	98	15 (15.3)	83 (84.7)	NE (22.7, NE)	43	6 (14.0)	37 (86.0)	NE (9.6, NE)	0.6228 (0.2342, 1.6561) 0.3426	0.3385	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2319
<65	289	38 (13.1)	251 (86.9)	NE (22.7, NE)	126	14 (11.1)	112 (88.9)	NE (11.5, NE)	0.6265 (0.3305, 1.1876) 0.1518	0.1487	
>=65	82	5 (6.1)	77 (93.9)	NE (NE, NE)	46	6 (13.0)	40 (87.0)	NE (9.6, NE)	0.2826 (0.0823, 0.9701) 0.0446	0.0333	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9421
<75	357	42 (11.8)	315 (88.2)	NE (22.7, NE)	163	19 (11.7)	144 (88.3)	NE (11.5, NE)	0.5209 (0.2941, 0.9226) 0.0253	0.0231	
>=75	14	1 (7.1)	13 (92.9)	NE (NE, NE)	9	1 (11.1)	8 (88.9)	NE (5.5, NE)	0.5025 (0.0313, 8.0623) 0.6270	0.6202	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.5133
White	175	25 (14.3)	150 (85.7)	22.7 (22.7, NE)	85	13 (15.3)	72 (84.7)	11.6 (11.5, NE)	0.3730 (0.1800, 0.7729) 0.0080	0.0060	
Non-White	196	18 (9.2)	178 (90.8)	NE (NE, NE)	86	7 (8.1)	79 (91.9)	NE (9.6, NE)	0.7716 (0.3158, 1.8854) 0.5696	0.5685	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.0540
Asia	147	12 (8.2)	135 (91.8)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (NE, NE)	3.8409 (0.4942, 29.8507) 0.1983	0.1665	
North America	58	10 (17.2)	48 (82.8)	NE (12.9, NE)	28	7 (25.0)	21 (75.0)	NE (2.7, NE)	0.2762 (0.0926, 0.8240) 0.0211	0.0143	
Europe + Israel	166	21 (12.7)	145 (87.3)	22.7 (22.7, NE)	81	12 (14.8)	69 (85.2)	11.6 (9.6, NE)	0.3698 (0.1727, 0.7917) 0.0104	0.0080	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.0027
0	199	22 (11.1)	177 (88.9)	NE (NE, NE)	95	17 (17.9)	78 (82.1)	11.6 (9.6, NE)	0.2977 (0.1521, 0.5825) 0.0004	0.0002	
1	172	21 (12.2)	151 (87.8)	22.7 (22.7, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	1.8758 (0.5455, 6.4499) 0.3182	0.3108	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.0610
0	60	5 (8.3)	55 (91.7)	NE (NE, NE)	31	1 (3.2)	30 (96.8)	NE (NE, NE)	1.4382 (0.1547, 13.3688) 0.7494	0.7480	
1	107	13 (12.1)	94 (87.9)	NE (NE, NE)	48	10 (20.8)	38 (79.2)	11.6 (11.5, NE)	0.3422 (0.1464, 0.7999) 0.0133	0.0098	
2	114	13 (11.4)	101 (88.6)	NE (22.7, NE)	50	8 (16.0)	42 (84.0)	9.6 (9.6, NE)	0.3980 (0.1542, 1.0275) 0.0569	0.0493	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	12 (13.3)	78 (86.7)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	2.7133 (0.3437, 21.4202) 0.3437	0.3248	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.7555
PD	173	22 (12.7)	151 (87.3)	NE (22.7, NE)	77	8 (10.4)	69 (89.6)	NE (NE, NE)	0.6652 (0.2868, 1.5429)	0.3402	
PR	48	4 (8.3)	44 (91.7)	NE (NE, NE)	21	2 (9.5)	19 (90.5)	9.6 (9.6, NE)	0.5292 (0.0879, 3.1847)	0.4805	
SD	82	8 (9.8)	74 (90.2)	NE (NE, NE)	54	7 (13.0)	47 (87.0)	NE (11.5, NE)	0.4421 (0.1530, 1.2776)	0.1230	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.0354
Yes	37	6 (16.2)	31 (83.8)	NE (16.2, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9956	0.2224	
No	334	37 (11.1)	297 (88.9)	NE (22.7, NE)	159	20 (12.6)	139 (87.4)	NE (11.5, NE)	0.4645 (0.2618, 0.8240) 0.0087	0.0074	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0448
Yes	24	5 (20.8)	19 (79.2)	NE (8.4, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9960	0.2697	
No	347	38 (11.0)	309 (89.0)	NE (22.7, NE)	165	20 (12.1)	145 (87.9)	NE (11.5, NE)	0.4597 (0.2593, 0.8149) 0.0078	0.0065	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.5245
Normal Function	201	22 (10.9)	179 (89.1)	NE (NE, NE)	80	6 (7.5)	74 (92.5)	NE (NE, NE)	0.8644 (0.3390, 2.2042) 0.7602	0.7611	
Mild Impairment	123	17 (13.8)	106 (86.2)	NE (22.7, NE)	65	9 (13.8)	56 (86.2)	11.5 (9.6, NE)	0.4769 (0.2016, 1.1284) 0.0920	0.0857	
Moderate Impairment	41	4 (9.8)	37 (90.2)	NE (NE, NE)	23	5 (21.7)	18 (78.3)	NE (5.5, NE)	0.2792 (0.0738, 1.0562) 0.0602	0.0454	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.7179
Normal Function	170	22 (12.9)	148 (87.1)	NE (22.7, NE)	88	12 (13.6)	76 (86.4)	NE (9.6, NE)	0.4945 (0.2357, 1.0375) 0.0625	0.0580	
Mild Impairment	194	21 (10.8)	173 (89.2)	NE (NE, NE)	82	8 (9.8)	74 (90.2)	NE (11.5, NE)	0.6003 (0.2567, 1.4039) 0.2390	0.2335	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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 [c] Two-sided p-value from unstratified log-rank test.  
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DE.T.4.8.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.8322
Yes	331	36 (10.9)	295 (89.1)	NE (22.7, NE)	146	17 (11.6)	129 (88.4)	NE (11.5, NE)	0.5068 (0.2775, 0.9255) 0.0270	0.0244	
No	40	7 (17.5)	33 (82.5)	NE (NE, NE)	26	3 (11.5)	23 (88.5)	NE (NE, NE)	0.8060 (0.1900, 3.4200) 0.7699	0.7696	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.9339
Positive	329	41 (12.5)	288 (87.5)	NE (22.7, NE)	152	19 (12.5)	133 (87.5)	NE (11.5, NE)	0.5428 (0.3077, 0.9576)	0.0324	
Negative	42	2 (4.8)	40 (95.2)	NE (10.8, NE)	20	1 (5.0)	19 (95.0)	NE (NE, NE)	0.4161 (0.0258, 6.7118)	0.5236	

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 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.2403
Positive	331	41 (12.4)	290 (87.6)	NE (22.7, NE)	155	20 (12.9)	135 (87.1)	NE (11.5, NE)	0.5238 (0.2996, 0.9159)	0.0212	
Negative	40	2 (5.0)	38 (95.0)	NE (10.8, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) 0.9981	0.5839	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Back pain

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.7623
HER2 IHC 1+	214	22 (10.3)	192 (89.7)	NE (NE, NE)	100	7 (7.0)	93 (93.0)	NE (11.8, NE)	1.0645 (0.4492, 2.5229) 0.8870	0.8873	
HER2 IHC 2+/ISH Negative	157	12 (7.6)	145 (92.4)	NE (NE, NE)	72	3 (4.2)	69 (95.8)	NE (NE, NE)	1.2083 (0.3340, 4.3714) 0.7730	0.7707	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.2711
1	220	24 (10.9)	196 (89.1)	NE (NE, NE)	94	5 (5.3)	89 (94.7)	NE (NE, NE)	1.6078 (0.6097, 4.2399) 0.3371	0.3325	
>=2	150	10 (6.7)	140 (93.3)	NE (NE, NE)	78	5 (6.4)	73 (93.6)	NE (11.8, NE)	0.5721 (0.1863, 1.7571) 0.3293	0.3239	

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Prior CDK4/6											0.1091
Yes	233	21 (9.0)	212 (91.0)	NE (NE, NE)	112	8 (7.1)	104 (92.9)	NE (NE, NE)	0.8509 (0.3706, 1.9536) 0.7034	0.7025	
No	98	12 (12.2)	86 (87.8)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (11.8, NE)	4.1144 (0.5308, 31.8897) 0.1758	0.1422	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
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Age											0.0297
<65	289	28 (9.7)	261 (90.3)	NE (NE, NE)	126	10 (7.9)	116 (92.1)	NE (11.8, NE)	0.8125 (0.3882, 1.7006) 0.5816	0.5811	
>=65	82	6 (7.3)	76 (92.7)	NE (NE, NE)	46	0	46 (100)	NE (NE, NE)	NE (NE, NE) 0.9946	0.1024	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											1.0000
<75	357	34 (9.5)	323 (90.5)	NE (NE, NE)	163	10 (6.1)	153 (93.9)	NE (11.8, NE)	1.0597 (0.5169, 2.1724) 0.8742	0.8737	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) NE		

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.5048
White	175	16 (9.1)	159 (90.9)	NE (NE, NE)	85	6 (7.1)	79 (92.9)	NE (NE, NE)	0.8943 (0.3429, 2.3328) 0.8194	0.8195	
Non-White	196	18 (9.2)	178 (90.8)	NE (NE, NE)	86	4 (4.7)	82 (95.3)	NE (11.8, NE)	1.4193 (0.4747, 4.2432) 0.5309	0.5286	

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 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.1180
Asia	147	15 (10.2)	132 (89.8)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (NE, NE)	4.7230 (0.6193, 36.0212) 0.1342	0.0989	
North America	58	8 (13.8)	50 (86.2)	NE (16.5, NE)	28	3 (10.7)	25 (89.3)	NE (NE, NE)	0.9416 (0.2390, 3.7097) 0.9314	0.9278	
Europe + Israel	166	11 (6.6)	155 (93.4)	NE (NE, NE)	81	6 (7.4)	75 (92.6)	NE (11.8, NE)	0.5824 (0.2107, 1.6094) 0.2972	0.2933	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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SOC: Musculoskeletal and connective tissue disorders; PT: Back pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.7411
0	199	19 (9.5)	180 (90.5)	NE (NE, NE)	95	5 (5.3)	90 (94.7)	NE (NE, NE)	1.2816 (0.4734, 3.4700) 0.6253	0.6239	
1	172	15 (8.7)	157 (91.3)	NE (NE, NE)	77	5 (6.5)	72 (93.5)	NE (11.8, NE)	0.9024 (0.3196, 2.5484) 0.8463	0.8457	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Back pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.0516
0	60	1 (1.7)	59 (98.3)	NE (NE, NE)	31	1 (3.2)	30 (96.8)	NE (NE, NE)	0.3326 (0.0193, 5.7186) 0.4482	0.4281	
1	107	8 (7.5)	99 (92.5)	NE (NE, NE)	48	4 (8.3)	44 (91.7)	NE (NE, NE)	0.7479 (0.2238, 2.4987) 0.6369	0.6358	
2	114	13 (11.4)	101 (88.6)	NE (NE, NE)	50	5 (10.0)	45 (90.0)	11.8 (NE, NE)	0.6638 (0.2232, 1.9735) 0.4610	0.4581	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Back pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	12 (13.3)	78 (86.7)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9933	0.0507	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Back pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.3096
PD	173	14 (8.1)	159 (91.9)	NE (NE, NE)	77	6 (7.8)	71 (92.2)	11.8 (11.8, NE)	0.5938 (0.2195, 1.6065)	0.3005	
PR	48	4 (8.3)	44 (91.7)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	0.3047 (NE, NE)	0.3591	
SD	82	4 (4.9)	78 (95.1)	NE (NE, NE)	54	2 (3.7)	52 (96.3)	NE (NE, NE)	1.1101 (0.2011, 6.1267)	0.9046	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Back pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.1935
Yes	37	4 (10.8)	33 (89.2)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9966	0.3564	
No	334	30 (9.0)	304 (91.0)	NE (NE, NE)	159	10 (6.3)	149 (93.7)	NE (NE, NE)	1.0162 (0.4912, 2.1023) 0.9655	0.9646	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Back pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.2416
Yes	24	3 (12.5)	21 (87.5)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9968	0.3726	
No	347	31 (8.9)	316 (91.1)	NE (NE, NE)	165	10 (6.1)	155 (93.9)	NE (NE, NE)	1.0083 (0.4884, 2.0818) 0.9822	0.9814	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Back pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.1037
Normal Function	201	16 (8.0)	185 (92.0)	NE (NE, NE)	80	7 (8.8)	73 (91.3)	NE (NE, NE)	0.6764 (0.2740, 1.6701) 0.3966	0.3949	
Mild Impairment	123	15 (12.2)	108 (87.8)	NE (NE, NE)	65	3 (4.6)	62 (95.4)	11.8 (11.8, NE)	1.4843 (0.4168, 5.2854) 0.5422	0.5399	
Moderate Impairment	41	3 (7.3)	38 (92.7)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9961	0.2320	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Back pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.0440
Normal Function	170	20 (11.8)	150 (88.2)	NE (NE, NE)	88	3 (3.4)	85 (96.6)	NE (NE, NE)	2.6127 (0.7695, 8.8714) 0.1236	0.1102	
Mild Impairment	194	14 (7.2)	180 (92.8)	NE (NE, NE)	82	7 (8.5)	75 (91.5)	NE (11.8, NE)	0.5157 (0.2019, 1.3173) 0.1664	0.1598	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Back pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.4217
Yes	331	28 (8.5)	303 (91.5)	NE (NE, NE)	146	9 (6.2)	137 (93.8)	NE (NE, NE)	0.9949 (0.4651, 2.1284) 0.9895	0.9905	
No	40	6 (15.0)	34 (85.0)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	2.2841 (0.2587, 20.1666) 0.4573	0.4456	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Back pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.0793
Positive	329	33 (10.0)	296 (90.0)	NE (NE, NE)	152	8 (5.3)	144 (94.7)	NE (NE, NE)	1.3468 (0.6161, 2.9443)	0.4535	
Negative	42	1 (2.4)	41 (97.6)	NE (NE, NE)	20	2 (10.0)	18 (90.0)	NE (NE, NE)	0.1415 (0.0113, 1.7705)	0.0871	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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SOC: Musculoskeletal and connective tissue disorders; PT: Back pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.3180
Positive	331	33 (10.0)	298 (90.0)	NE (NE, NE)	155	9 (5.8)	146 (94.2)	NE (NE, NE)	1.2179 (0.5769, 2.5711)	0.6044	
Negative	40	1 (2.5)	39 (97.5)	NE (NE, NE)	17	1 (5.9)	16 (94.1)	NE (NE, NE)	0.2287 (0.0124, 4.2286)	0.2876	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.7209
HER2 IHC 1+	214	15 (7.0)	199 (93.0)	NE (NE, NE)	100	3 (3.0)	97 (97.0)	NE (NE, NE)	1.4725 (0.4156, 5.2166) 0.5488	0.5461	
HER2 IHC 2+/ISH Negative	157	14 (8.9)	143 (91.1)	NE (NE, NE)	72	2 (2.8)	70 (97.2)	NE (NE, NE)	1.9252 (0.4280, 8.6595) 0.3932	0.3852	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.0249
1	220	17 (7.7)	203 (92.3)	NE (NE, NE)	94	5 (5.3)	89 (94.7)	NE (NE, NE)	0.9268 (0.3341, 2.5711) 0.8839	0.8839	
>=2	150	11 (7.3)	139 (92.7)	NE (NE, NE)	78	0	78 (100)	NE (NE, NE)	NE (NE, NE) 0.9938	0.0705	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.5497
Yes	233	19 (8.2)	214 (91.8)	NE (NE, NE)	112	4 (3.6)	108 (96.4)	NE (NE, NE)	1.3380 (0.4404, 4.0646) 0.6075	0.6065	
No	98	9 (9.2)	89 (90.8)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	2.8988 (0.3651, 23.0185) 0.3141	0.2917	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7455
<65	289	26 (9.0)	263 (91.0)	NE (NE, NE)	126	4 (3.2)	122 (96.8)	NE (NE, NE)	1.6801 (0.5746, 4.9122) 0.3432	0.3381	
>=65	82	3 (3.7)	79 (96.3)	NE (NE, NE)	46	1 (2.2)	45 (97.8)	NE (NE, NE)	1.3569 (0.1380, 13.3426) 0.7936	0.7928	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2226
<75	357	27 (7.6)	330 (92.4)	NE (NE, NE)	163	5 (3.1)	158 (96.9)	NE (NE, NE)	1.4506 (0.5467, 3.8490) 0.4550	0.4521	
>=75	14	2 (14.3)	12 (85.7)	NE (7.8, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9979	0.2757	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.4523
White	175	18 (10.3)	157 (89.7)	NE (NE, NE)	85	4 (4.7)	81 (95.3)	NE (NE, NE)	1.3068 (0.4309, 3.9634) 0.6364	0.6358	
Non-White	196	11 (5.6)	185 (94.4)	NE (NE, NE)	86	1 (1.2)	85 (98.8)	NE (NE, NE)	3.0025 (0.3802, 23.7099) 0.2971	0.2738	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.3681
Asia	147	6 (4.1)	141 (95.9)	NE (NE, NE)	63	0	63 (100)	NE (NE, NE)	NE (NE, NE) 0.9954	0.1964	
North America	58	7 (12.1)	51 (87.9)	NE (15.9, NE)	28	1 (3.6)	27 (96.4)	NE (NE, NE)	0.9903 (0.0979, 10.0186) 0.9934	0.9934	
Europe + Israel	166	16 (9.6)	150 (90.4)	NE (NE, NE)	81	4 (4.9)	77 (95.1)	NE (NE, NE)	1.3427 (0.4408, 4.0900) 0.6041	0.6031	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.0676
0	199	18 (9.0)	181 (91.0)	NE (NE, NE)	95	1 (1.1)	94 (98.9)	NE (NE, NE)	4.8591 (0.6406, 36.8560) 0.1262	0.0913	
1	172	11 (6.4)	161 (93.6)	NE (NE, NE)	77	4 (5.2)	73 (94.8)	NE (NE, NE)	0.8205 (0.2509, 2.6829) 0.7434	0.7431	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.9179
0	60	3 (5.0)	57 (95.0)	NE (NE, NE)	31	1 (3.2)	30 (96.8)	NE (NE, NE)	0.9238 (0.0885, 9.6452) 0.9472	0.9472	
1	107	13 (12.1)	94 (87.9)	NE (NE, NE)	48	2 (4.2)	46 (95.8)	NE (NE, NE)	2.2978 (0.5151, 10.2509) 0.2755	0.2621	
2	114	5 (4.4)	109 (95.6)	NE (NE, NE)	50	1 (2.0)	49 (98.0)	NE (NE, NE)	0.7617 (0.0754, 7.6899) 0.8175	0.8171	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	8 (8.9)	82 (91.1)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	2.1729 (0.2620, 18.0190) 0.4721	0.4615	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.1761
PD	173	10 (5.8)	163 (94.2)	NE (NE, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	1.4345 (0.3043, 6.7631)	0.6469	
PR	48	5 (10.4)	43 (89.6)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	0.6484 (NE, NE)	0.2478	
SD	82	3 (3.7)	79 (96.3)	NE (NE, NE)	54	3 (5.6)	51 (94.4)	NE (NE, NE)	0.9959 (0.1099, 2.8154)	0.4725	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.2797
Yes	37	4 (10.8)	33 (89.2)	NE (16.2, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9963	0.2995	
No	334	25 (7.5)	309 (92.5)	NE (NE, NE)	159	5 (3.1)	154 (96.9)	NE (NE, NE)	1.4596 (0.5478, 3.8893) 0.4495	0.4465	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.4292
Yes	24	2 (8.3)	22 (91.7)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9973	0.4452	
No	347	27 (7.8)	320 (92.2)	NE (NE, NE)	165	5 (3.0)	160 (97.0)	NE (NE, NE)	1.5213 (0.5733, 4.0367) 0.3994	0.3957	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.6230
Normal Function	201	21 (10.4)	180 (89.6)	NE (NE, NE)	80	3 (3.8)	77 (96.3)	NE (NE, NE)	1.6341 (0.4756, 5.6147) 0.4355	0.4311	
Mild Impairment	123	6 (4.9)	117 (95.1)	NE (NE, NE)	65	2 (3.1)	63 (96.9)	NE (NE, NE)	0.6938 (0.1274, 3.7793) 0.6725	0.6713	
Moderate Impairment	41	1 (2.4)	40 (97.6)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9977	0.4539	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.9391
Normal Function	170	15 (8.8)	155 (91.2)	NE (NE, NE)	88	3 (3.4)	85 (96.6)	NE (NE, NE)	1.5237 (0.4298, 5.4024) 0.5143	0.5109	
Mild Impairment	194	13 (6.7)	181 (93.3)	NE (NE, NE)	82	2 (2.4)	80 (97.6)	NE (NE, NE)	1.6272 (0.3568, 7.4209) 0.5295	0.5256	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.4039
Yes	331	27 (8.2)	304 (91.8)	NE (NE, NE)	146	5 (3.4)	141 (96.6)	NE (NE, NE)	1.4559 (0.5520, 3.8398) 0.4478	0.4448	
No	40	2 (5.0)	38 (95.0)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9966	0.2481	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.3848
Positive	329	27 (8.2)	302 (91.8)	NE (NE, NE)	152	4 (2.6)	148 (97.4)	NE (NE, NE)	1.9095 (0.6578, 5.5429)	0.2265	
Negative	42	2 (4.8)	40 (95.2)	NE (NE, NE)	20	1 (5.0)	19 (95.0)	NE (NE, NE)	0.4939 (0.0309, 7.8964)	0.6106	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.5967
Positive	331	28 (8.5)	303 (91.5)	NE (NE, NE)	155	5 (3.2)	150 (96.8)	NE (NE, NE)	1.6514 (0.6274, 4.3464)	0.3049	
Negative	40	1 (2.5)	39 (97.5)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.2275
HER2 IHC 1+	214	8 (3.7)	206 (96.3)	NE (NE, NE)	100	9 (9.0)	91 (91.0)	NE (NE, NE)	0.2654 (0.0980, 0.7184) 0.0090	0.0055	
HER2 IHC 2+/ISH Negative	157	14 (8.9)	143 (91.1)	NE (NE, NE)	72	7 (9.7)	65 (90.3)	NE (11.0, NE)	0.6148 (0.2413, 1.5664) 0.3079	0.3045	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.7273
1	220	17 (7.7)	203 (92.3)	NE (NE, NE)	94	11 (11.7)	83 (88.3)	NE (11.0, NE)	0.4174 (0.1894, 0.9201) 0.0303	0.0258	
>=2	150	5 (3.3)	145 (96.7)	NE (NE, NE)	78	5 (6.4)	73 (93.6)	NE (NE, NE)	0.3571 (0.0975, 1.3075) 0.1199	0.1061	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.5861
Yes	233	14 (6.0)	219 (94.0)	NE (NE, NE)	112	10 (8.9)	102 (91.1)	NE (11.0, NE)	0.3731 (0.1578, 0.8822) 0.0247	0.0203	
No	98	6 (6.1)	92 (93.9)	NE (NE, NE)	43	6 (14.0)	37 (86.0)	NE (NE, NE)	0.3413 (0.1084, 1.0742) 0.0661	0.0545	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6305
<65	289	18 (6.2)	271 (93.8)	NE (NE, NE)	126	11 (8.7)	115 (91.3)	NE (11.0, NE)	0.4400 (0.2004, 0.9658) 0.0407	0.0360	
>=65	82	4 (4.9)	78 (95.1)	NE (NE, NE)	46	5 (10.9)	41 (89.1)	NE (NE, NE)	0.3494 (0.0926, 1.3181) 0.1206	0.1050	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1649
<75	357	21 (5.9)	336 (94.1)	NE (NE, NE)	163	16 (9.8)	147 (90.2)	NE (11.0, NE)	0.3719 (0.1879, 0.7363) 0.0045	0.0033	
>=75	14	1 (7.1)	13 (92.9)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9985	0.4328	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.3635
White	175	11 (6.3)	164 (93.7)	NE (NE, NE)	85	6 (7.1)	79 (92.9)	NE (11.0, NE)	0.5240 (0.1865, 1.4727) 0.2203	0.2133	
Non-White	196	11 (5.6)	185 (94.4)	NE (NE, NE)	86	10 (11.6)	76 (88.4)	NE (NE, NE)	0.3387 (0.1391, 0.8250) 0.0171	0.0128	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.6764
Asia	147	6 (4.1)	141 (95.9)	NE (NE, NE)	63	6 (9.5)	57 (90.5)	NE (NE, NE)	0.3855 (0.1234, 1.2045) 0.1010	0.0890	
North America	58	3 (5.2)	55 (94.8)	NE (NE, NE)	28	2 (7.1)	26 (92.9)	NE (6.1, NE)	0.2478 (0.0335, 1.8353) 0.1721	0.1416	
Europe + Israel	166	13 (7.8)	153 (92.2)	NE (NE, NE)	81	8 (9.9)	73 (90.1)	NE (11.0, NE)	0.4842 (0.1936, 1.2109) 0.1210	0.1140	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.8901
0	199	13 (6.5)	186 (93.5)	NE (NE, NE)	95	9 (9.5)	86 (90.5)	NE (11.0, NE)	0.4333 (0.1797, 1.0447) 0.0625	0.0566	
1	172	9 (5.2)	163 (94.8)	NE (NE, NE)	77	7 (9.1)	70 (90.9)	NE (NE, NE)	0.4161 (0.1500, 1.1547) 0.0922	0.0827	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.2402
0	60	4 (6.7)	56 (93.3)	NE (NE, NE)	31	1 (3.2)	30 (96.8)	NE (NE, NE)	1.7176 (0.1894, 15.5772) 0.6306	0.6246	
1	107	3 (2.8)	104 (97.2)	NE (NE, NE)	48	7 (14.6)	41 (85.4)	NE (11.0, NE)	0.1391 (0.0348, 0.5554) 0.0052	0.0013	
2	114	8 (7.0)	106 (93.0)	NE (NE, NE)	50	4 (8.0)	46 (92.0)	NE (NE, NE)	0.5401 (0.1550, 1.8824) 0.3336	0.3273	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	7 (7.8)	83 (92.2)	NE (NE, NE)	43	4 (9.3)	39 (90.7)	NE (6.1, NE)	0.4539 (0.1232, 1.6721) 0.2351	0.2250	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.3624
PD	173	11 (6.4)	162 (93.6)	NE (NE, NE)	77	4 (5.2)	73 (94.8)	NE (NE, NE)	0.8597 (0.2665, 2.7739)	0.8005	
PR	48	3 (6.3)	45 (93.8)	NE (NE, NE)	21	3 (14.3)	18 (85.7)	NE (6.8, NE)	0.3358 (0.0653, 1.7276)	0.1716	
SD	82	5 (6.1)	77 (93.9)	NE (NE, NE)	54	7 (13.0)	47 (87.0)	NE (11.0, NE)	0.3237 (0.0994, 1.0539)	0.0498	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.0820
Yes	37	3 (8.1)	34 (91.9)	NE (12.1, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9969	0.3947	
No	334	19 (5.7)	315 (94.3)	NE (NE, NE)	159	16 (10.1)	143 (89.9)	NE (NE, NE)	0.3668 (0.1833, 0.7338) 0.0046	0.0033	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.3244
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9981	0.6080	
No	347	21 (6.1)	326 (93.9)	NE (NE, NE)	165	16 (9.7)	149 (90.3)	NE (NE, NE)	0.3969 (0.2011, 0.7833) 0.0077	0.0060	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0202
Normal Function	201	11 (5.5)	190 (94.5)	NE (NE, NE)	80	8 (10.0)	72 (90.0)	NE (NE, NE)	0.3454 (0.1309, 0.9113) 0.0318	0.0252	
Mild Impairment	123	4 (3.3)	119 (96.7)	NE (NE, NE)	65	6 (9.2)	59 (90.8)	11.0 (11.0, NE)	0.1474 (0.0360, 0.6038) 0.0078	0.0030	
Moderate Impairment	41	7 (17.1)	34 (82.9)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	3.5581 (0.4368, 28.9849) 0.2356	0.2052	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1718
Normal Function	170	8 (4.7)	162 (95.3)	NE (NE, NE)	88	10 (11.4)	78 (88.6)	NE (NE, NE)	0.2856 (0.1101, 0.7409) 0.0100	0.0063	
Mild Impairment	194	14 (7.2)	180 (92.8)	NE (NE, NE)	82	6 (7.3)	76 (92.7)	NE (11.0, NE)	0.6020 (0.2204, 1.6442) 0.3222	0.3175	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.0410
Yes	331	19 (5.7)	312 (94.3)	NE (NE, NE)	146	16 (11.0)	130 (89.0)	NE (NE, NE)	0.3398 (0.1702, 0.6782) 0.0022	0.0014	
No	40	3 (7.5)	37 (92.5)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9962	0.2360	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.0508
Positive	329	19 (5.8)	310 (94.2)	NE (NE, NE)	152	16 (10.5)	136 (89.5)	NE (NE, NE)	0.3436 (0.1720, 0.6864)	0.0016	
Negative	42	3 (7.1)	39 (92.9)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) 0.9961	0.2241	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.3085
Positive	331	21 (6.3)	310 (93.7)	NE (NE, NE)	155	16 (10.3)	139 (89.7)	NE (NE, NE)	0.3983 (0.2028, 0.7821)	0.0058	
Negative	40	1 (2.5)	39 (97.5)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) 0.9978	0.5145	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Muscle spasms

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.5306
HER2 IHC 1+	214	9 (4.2)	205 (95.8)	NE (NE, NE)	100	1 (1.0)	99 (99.0)	NE (NE, NE)	2.1076 (0.2559, 17.3556) 0.4882	0.4786	
HER2 IHC 2+/ISH Negative	157	8 (5.1)	149 (94.9)	NE (NE, NE)	72	2 (2.8)	70 (97.2)	NE (NE, NE)	1.3072 (0.2738, 6.2414) 0.7370	0.7362	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Muscle spasms

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.8572
1	220	5 (2.3)	215 (97.7)	NE (NE, NE)	94	1 (1.1)	93 (98.9)	NE (NE, NE)	1.1802 (0.1326, 10.5036) 0.8819	0.8818	
>=2	150	12 (8.0)	138 (92.0)	NE (NE, NE)	78	2 (2.6)	76 (97.4)	NE (NE, NE)	1.8843 (0.4114, 8.6302) 0.4145	0.4070	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Muscle spasms

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.0843
Yes	233	14 (6.0)	219 (94.0)	NE (NE, NE)	112	1 (0.9)	111 (99.1)	NE (NE, NE)	3.9910 (0.5148, 30.9412) 0.1853	0.1529	
No	98	3 (3.1)	95 (96.9)	NE (NE, NE)	43	2 (4.7)	41 (95.3)	NE (NE, NE)	0.4794 (0.0795, 2.8887) 0.4223	0.4121	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Muscle spasms

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0443
<65	289	10 (3.5)	279 (96.5)	NE (NE, NE)	126	3 (2.4)	123 (97.6)	NE (NE, NE)	0.7618 (0.2027, 2.8628) 0.6870	0.6863	
>=65	82	7 (8.5)	75 (91.5)	NE (NE, NE)	46	0	46 (100)	NE (NE, NE)	NE (NE, NE) 0.9942	0.0738	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Muscle spasms

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4159
<75	357	16 (4.5)	341 (95.5)	NE (NE, NE)	163	3 (1.8)	160 (98.2)	NE (NE, NE)	1.4053 (0.4010, 4.9242) 0.5948	0.5929	
>=75	14	1 (7.1)	13 (92.9)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9985	0.4227	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Muscle spasms

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.9701
White	175	11 (6.3)	164 (93.7)	NE (NE, NE)	85	2 (2.4)	83 (97.6)	NE (NE, NE)	1.7996 (0.3928, 8.2448) 0.4493	0.4429	
Non-White	196	6 (3.1)	190 (96.9)	NE (NE, NE)	86	1 (1.2)	85 (98.8)	NE (NE, NE)	1.3567 (0.1565, 11.7611) 0.7819	0.7810	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Muscle spasms

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.2884
Asia	147	1 (0.7)	146 (99.3)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (NE, NE)	0.3217 (0.0196, 5.2735) 0.4268	0.4031	
North America	58	3 (5.2)	55 (94.8)	NE (17.5, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9964	0.5391	
Europe + Israel	166	13 (7.8)	153 (92.2)	NE (NE, NE)	81	2 (2.5)	79 (97.5)	NE (NE, NE)	2.2004 (0.4893, 9.8955) 0.3039	0.2919	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Muscle spasms

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.7765
0	199	10 (5.0)	189 (95.0)	NE (NE, NE)	95	2 (2.1)	93 (97.9)	NE (NE, NE)	1.3262 (0.2850, 6.1708) 0.7189	0.7179	
1	172	7 (4.1)	165 (95.9)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	2.1954 (0.2630, 18.3248) 0.4676	0.4566	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Muscle spasms

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1564
0	60	0	60 (100)	NE (NE, NE)	31	1 (3.2)	30 (96.8)	NE (NE, NE)	0.0000 (0.0000, ) 0.9977	0.1466	
1	107	4 (3.7)	103 (96.3)	NE (NE, NE)	48	1 (2.1)	47 (97.9)	NE (NE, NE)	1.1571 (0.1240, 10.7997) 0.8981	0.8980	
2	114	8 (7.0)	106 (93.0)	NE (NE, NE)	50	1 (2.0)	49 (98.0)	NE (NE, NE)	1.7494 (0.2067, 14.8037) 0.6078	0.6033	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Muscle spasms

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	5 (5.6)	85 (94.4)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9957	0.2218	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Muscle spasms

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.3531
PD	173	8 (4.6)	165 (95.4)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE) 0.9949	0.1421	
PR	48	2 (4.2)	46 (95.8)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	NE (NE, NE) 0.9972	0.4149	
SD	82	3 (3.7)	79 (96.3)	NE (NE, NE)	54	1 (1.9)	53 (98.1)	NE (NE, NE)	1.5899 (0.1645, 15.3648) 0.6887	0.6859	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Muscle spasms

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.2664
Yes	37	2 (5.4)	35 (94.6)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (3.5, NE)	0.5477 (0.0486, 6.1718)	0.6211	
No	334	15 (4.5)	319 (95.5)	NE (NE, NE)	159	2 (1.3)	157 (98.7)	NE (NE, NE)	2.0968 (0.4705, 9.3438)	0.3209	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Muscle spasms

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.6012
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9981	0.5892	
No	347	16 (4.6)	331 (95.4)	NE (NE, NE)	165	3 (1.8)	162 (98.2)	NE (NE, NE)	1.4862 (0.4249, 5.1985) 0.5351	0.5321	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Muscle spasms

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.9976
Normal Function	201	7 (3.5)	194 (96.5)	NE (NE, NE)	80	1 (1.3)	79 (98.8)	NE (NE, NE)	1.2376 (0.1459, 10.5017) 0.8451	0.8447	
Mild Impairment	123	6 (4.9)	117 (95.1)	NE (NE, NE)	65	1 (1.5)	64 (98.5)	NE (NE, NE)	2.2621 (0.2695, 18.9899) 0.4521	0.4398	
Moderate Impairment	41	4 (9.8)	37 (90.2)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	1.9427 (0.2158, 17.4852) 0.5536	0.5464	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Muscle spasms

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.2948
Normal Function	170	5 (2.9)	165 (97.1)	NE (NE, NE)	88	2 (2.3)	86 (97.7)	NE (NE, NE)	0.6641 (0.1230, 3.5865) 0.6343	0.6324	
Mild Impairment	194	12 (6.2)	182 (93.8)	NE (NE, NE)	82	1 (1.2)	81 (98.8)	NE (NE, NE)	3.2984 (0.4228, 25.7324) 0.2549	0.2277	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Muscle spasms

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.5464
Yes	331	16 (4.8)	315 (95.2)	NE (NE, NE)	146	3 (2.1)	143 (97.9)	NE (NE, NE)	1.5052 (0.4315, 5.2509) 0.5212	0.5179	
No	40	1 (2.5)	39 (97.5)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9982	0.6121	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Muscle spasms

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.9999
Positive	329	17 (5.2)	312 (94.8)	NE (NE, NE)	152	3 (2.0)	149 (98.0)	NE (NE, NE)	1.6307 (0.4704, 5.6527)	0.4363	
Negative	42	0	42 (100)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Muscle spasms

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.9999
Positive	331	17 (5.1)	314 (94.9)	NE (NE, NE)	155	3 (1.9)	152 (98.1)	NE (NE, NE)	1.6595 (0.4786, 5.7544)	0.4199	
Negative	40	0	40 (100)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Bone pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.9386
HER2 IHC 1+	214	9 (4.2)	205 (95.8)	NE (NE, NE)	100	5 (5.0)	95 (95.0)	NE (NE, NE)	0.6670 (0.2208, 2.0153) 0.4729	0.4698	
HER2 IHC 2+/ISH Negative	157	5 (3.2)	152 (96.8)	NE (NE, NE)	72	3 (4.2)	69 (95.8)	NE (NE, NE)	0.5151 (0.1187, 2.2342) 0.3755	0.3689	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.7642
1	220	10 (4.5)	210 (95.5)	NE (NE, NE)	94	5 (5.3)	89 (94.7)	NE (NE, NE)	0.6365 (0.2146, 1.8873) 0.4153	0.4130	
>=2	150	4 (2.7)	146 (97.3)	NE (NE, NE)	78	3 (3.8)	75 (96.2)	NE (NE, NE)	0.5679 (0.1220, 2.6444) 0.4710	0.4668	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.3596
Yes	233	7 (3.0)	226 (97.0)	NE (NE, NE)	112	6 (5.4)	106 (94.6)	NE (NE, NE)	0.4369 (0.1437, 1.3282) 0.1444	0.1341	
No	98	6 (6.1)	92 (93.9)	NE (NE, NE)	43	2 (4.7)	41 (95.3)	NE (NE, NE)	0.9532 (0.1896, 4.7917) 0.9536	0.9536	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Age											0.3820
<65	289	13 (4.5)	276 (95.5)	NE (NE, NE)	126	6 (4.8)	120 (95.2)	NE (NE, NE)	0.6565 (0.2447, 1.7612) 0.4032	0.4007	
>=65	82	1 (1.2)	81 (98.8)	NE (NE, NE)	46	2 (4.3)	44 (95.7)	NE (NE, NE)	0.2723 (0.0247, 3.0038) 0.2882	0.2549	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Age											0.9998
<75	357	14 (3.9)	343 (96.1)	NE (NE, NE)	163	8 (4.9)	155 (95.1)	NE (NE, NE)	0.5859 (0.2416, 1.4209) 0.2369	0.2325	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.6894
White	175	8 (4.6)	167 (95.4)	NE (NE, NE)	85	4 (4.7)	81 (95.3)	NE (NE, NE)	0.7144 (0.2102, 2.4280) 0.5900	0.5900	
Non-White	196	6 (3.1)	190 (96.9)	NE (NE, NE)	86	4 (4.7)	82 (95.3)	NE (NE, NE)	0.5103 (0.1414, 1.8416) 0.3042	0.2964	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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SOC: Musculoskeletal and connective tissue disorders; PT: Bone pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.5006
Asia	147	5 (3.4)	142 (96.6)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (NE, NE)	1.4880 (0.1702, 13.0096) 0.7194	0.7165	
North America	58	3 (5.2)	55 (94.8)	NE (NE, NE)	28	3 (10.7)	25 (89.3)	NE (NE, NE)	0.4293 (0.0863, 2.1362) 0.3017	0.2903	
Europe + Israel	166	6 (3.6)	160 (96.4)	NE (NE, NE)	81	4 (4.9)	77 (95.1)	NE (NE, NE)	0.5266 (0.1444, 1.9213) 0.3315	0.3242	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Bone pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.6741
0	199	10 (5.0)	189 (95.0)	NE (NE, NE)	95	5 (5.3)	90 (94.7)	NE (NE, NE)	0.6518 (0.2190, 1.9397) 0.4417	0.4396	
1	172	4 (2.3)	168 (97.7)	NE (NE, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	0.5027 (0.1089, 2.3209) 0.3782	0.3709	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Bone pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1558
0	60	4 (6.7)	56 (93.3)	NE (NE, NE)	31	0	31 (100)	NE (NE, NE)	NE (NE, NE) 0.9959	0.2053	
1	107	2 (1.9)	105 (98.1)	NE (NE, NE)	48	3 (6.3)	45 (93.8)	NE (NE, NE)	0.2508 (0.0417, 1.5092) 0.1309	0.1028	
2	114	4 (3.5)	110 (96.5)	NE (NE, NE)	50	3 (6.0)	47 (94.0)	NE (NE, NE)	0.4164 (0.0881, 1.9681) 0.2689	0.2551	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Bone pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	4 (4.4)	86 (95.6)	NE (NE, NE)	43	2 (4.7)	41 (95.3)	NE (NE, NE)	0.6168 (0.1071, 3.5519) 0.5885	0.5855	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Bone pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.3112
PD	173	6 (3.5)	167 (96.5)	NE (NE, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	0.9844 (0.1940, 4.9954)	0.9849	
PR	48	2 (4.2)	46 (95.8)	NE (NE, NE)	21	3 (14.3)	18 (85.7)	NE (NE, NE)	0.2061 (0.0315, 1.3504)	0.0736	
SD	82	2 (2.4)	80 (97.6)	NE (NE, NE)	54	1 (1.9)	53 (98.1)	NE (NE, NE)	0.9922 (0.0887, 11.0968)	0.9949	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Bone pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.8654
Yes	37	2 (5.4)	35 (94.6)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	0.5486 (0.0478, 6.2993)	0.6249	
No	334	12 (3.6)	322 (96.4)	NE (NE, NE)	159	7 (4.4)	152 (95.6)	NE (NE, NE)	0.5987 (0.2314, 1.5490)	0.2857	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Bone pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.4849
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	1 (14.3)	6 (85.7)	NE (0.3, NE)	0.2269 (0.0139, 3.7074) 0.2980	0.2563	
No	347	13 (3.7)	334 (96.3)	NE (NE, NE)	165	7 (4.2)	158 (95.8)	NE (NE, NE)	0.6626 (0.2600, 1.6887) 0.3885	0.3858	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0140
Normal Function	201	11 (5.5)	190 (94.5)	NE (NE, NE)	80	3 (3.8)	77 (96.3)	NE (NE, NE)	1.0084 (0.2765, 3.6777) 0.9899	0.9895	
Mild Impairment	123	1 (0.8)	122 (99.2)	NE (NE, NE)	65	5 (7.7)	60 (92.3)	NE (NE, NE)	0.1039 (0.0121, 0.8896) 0.0388	0.0113	
Moderate Impairment	41	2 (4.9)	39 (95.1)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9970	0.3620	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Bone pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.0805
Normal Function	170	8 (4.7)	162 (95.3)	NE (NE, NE)	88	2 (2.3)	86 (97.7)	NE (NE, NE)	1.4496 (0.3024, 6.9476) 0.6424	0.6403	
Mild Impairment	194	6 (3.1)	188 (96.9)	NE (NE, NE)	82	6 (7.3)	76 (92.7)	NE (NE, NE)	0.3374 (0.1066, 1.0681) 0.0646	0.0532	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Musculoskeletal and connective tissue disorders; PT: Bone pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1326
Yes	331	12 (3.6)	319 (96.4)	NE (NE, NE)	146	8 (5.5)	138 (94.5)	NE (NE, NE)	0.5171 (0.2090, 1.2792) 0.1535	0.1468	
No	40	2 (5.0)	38 (95.0)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9974	0.4043	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Bone pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.3261
Positive	329	13 (4.0)	316 (96.0)	NE (NE, NE)	152	8 (5.3)	144 (94.7)	NE (NE, NE)	0.5556 (0.2269, 1.3607)	0.1932	
Negative	42	1 (2.4)	41 (97.6)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) 0.9978	0.4849	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Musculoskeletal and connective tissue disorders; PT: Bone pain

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.3598
Positive	331	13 (3.9)	318 (96.1)	NE (NE, NE)	155	8 (5.2)	147 (94.8)	NE (NE, NE)	0.5649 (0.2306, 1.3838)	0.2065	
Negative	40	1 (2.5)	39 (97.5)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	0.2116 (NE, NE) 0.9978	0.5091	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.6087
HER2 IHC 1+	214	70 (32.7)	144 (67.3)	21.3 (12.7, NE)	100	18 (18.0)	82 (82.0)	NE (NE, NE)	1.2648 (0.7463, 2.1434) 0.3828	0.3827	
HER2 IHC 2+/ISH Negative	157	57 (36.3)	100 (63.7)	12.7 (8.9, NE)	72	18 (25.0)	54 (75.0)	NE (NE, NE)	1.0006 (0.5844, 1.7130) 0.9984	0.9969	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.0619
1	220	72 (32.7)	148 (67.3)	18.0 (12.3, NE)	94	14 (14.9)	80 (85.1)	NE (NE, NE)	1.6332 (0.9158, 2.9126) 0.0965	0.0936	
>=2	150	55 (36.7)	95 (63.3)	12.8 (9.7, NE)	78	22 (28.2)	56 (71.8)	NE (6.3, NE)	0.8147 (0.4895, 1.3558) 0.4303	0.4283	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.1158
Yes	233	77 (33.0)	156 (67.0)	18.0 (12.2, NE)	112	16 (14.3)	96 (85.7)	NE (7.1, NE)	1.5173 (0.8744, 2.6328) 0.1382	0.1355	
No	98	29 (29.6)	69 (70.4)	NE (12.8, NE)	43	12 (27.9)	31 (72.1)	NE (NE, NE)	0.7726 (0.3931, 1.5188) 0.4544	0.4539	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5366
<65	289	96 (33.2)	193 (66.8)	18.6 (12.4, NE)	126	26 (20.6)	100 (79.4)	NE (NE, NE)	1.0740 (0.6907, 1.6700) 0.7514	0.7527	
>=65	82	31 (37.8)	51 (62.2)	12.7 (8.1, NE)	46	10 (21.7)	36 (78.3)	NE (6.3, NE)	1.3532 (0.6583, 2.7813) 0.4107	0.4078	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7807
<75	357	121 (33.9)	236 (66.1)	18.0 (12.4, NE)	163	33 (20.2)	130 (79.8)	NE (NE, NE)	1.1222 (0.7577, 1.6619) 0.5651	0.5666	
>=75	14	6 (42.9)	8 (57.1)	6.5 (3.0, NE)	9	3 (33.3)	6 (66.7)	NE (0.6, NE)	1.2545 (0.3124, 5.0381) 0.7493	0.7488	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.6617
White	175	58 (33.1)	117 (66.9)	18.6 (12.2, NE)	85	17 (20.0)	68 (80.0)	NE (7.1, NE)	1.0126 (0.5811, 1.7645) 0.9647	0.9649	
Non-White	196	69 (35.2)	127 (64.8)	14.9 (11.7, NE)	86	18 (20.9)	68 (79.1)	NE (NE, NE)	1.2943 (0.7666, 2.1853) 0.3343	0.3328	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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[c] Two-sided p-value from unstratified log-rank test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.9280
Asia	147	49 (33.3)	98 (66.7)	NE (11.9, NE)	63	13 (20.6)	50 (79.4)	NE (NE, NE)	1.2051 (0.6500, 2.2341) 0.5536	0.5519	
North America	58	24 (41.4)	34 (58.6)	18.0 (5.5, NE)	28	6 (21.4)	22 (78.6)	NE (3.1, NE)	1.3091 (0.5240, 3.2709) 0.5642	0.5669	
Europe + Israel	166	54 (32.5)	112 (67.5)	18.6 (12.2, NE)	81	17 (21.0)	64 (79.0)	NE (NE, NE)	1.0165 (0.5824, 1.7739) 0.9542	0.9566	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.7299
0	199	68 (34.2)	131 (65.8)	18.0 (12.2, NE)	95	20 (21.1)	75 (78.9)	NE (NE, NE)	1.0644 (0.6409, 1.7676) 0.8096	0.8102	
1	172	59 (34.3)	113 (65.7)	21.3 (11.5, NE)	77	16 (20.8)	61 (79.2)	NE (NE, NE)	1.2240 (0.6980, 2.1465) 0.4806	0.4817	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.3907
0	60	28 (46.7)	32 (53.3)	8.0 (4.3, NE)	31	13 (41.9)	18 (58.1)	4.4 (2.3, NE)	0.7734 (0.3973, 1.5056) 0.4496	0.4474	
1	107	33 (30.8)	74 (69.2)	NE (12.7, NE)	48	9 (18.8)	39 (81.3)	NE (NE, NE)	1.3543 (0.6450, 2.8439) 0.4230	0.4214	
2	114	38 (33.3)	76 (66.7)	12.8 (11.5, NE)	50	10 (20.0)	40 (80.0)	NE (7.1, NE)	0.9475 (0.4606, 1.9493) 0.8836	0.8838	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]		
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	28 (31.1)	62 (68.9)	43	4 (9.3)	39 (90.7)	18.6 (14.9, NE)	NE (NE, NE)	2.1025 (0.7228, 6.1157) 0.1726	0.1631

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.9388
PD	173	53 (30.6)	120 (69.4)	18.6 (12.7, NE)	77	17 (22.1)	60 (77.9)	NE (7.1, NE)	0.9293 (0.5307, 1.6274)	0.7965	
PR	48	14 (29.2)	34 (70.8)	NE (11.7, NE)	21	3 (14.3)	18 (85.7)	NE (NE, NE)	0.7976 (0.4298, 5.3279)	0.5170	
SD	82	32 (39.0)	50 (61.0)	12.8 (9.7, NE)	54	14 (25.9)	40 (74.1)	NE (4.4, NE)	1.0423 (0.5500, 1.9752)	0.8982	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.5325
Yes	37	12 (32.4)	25 (67.6)	18.6 (5.0, NE)	13	3 (23.1)	10 (76.9)	NE (0.7, NE)	0.8291 (0.2253, 3.0506)	0.7819	
No	334	115 (34.4)	219 (65.6)	18.0 (12.3, NE)	159	33 (20.8)	126 (79.2)	NE (NE, NE)	0.7780 (0.7846, 1.7224)	0.4540	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.4643
Yes	24	7 (29.2)	17 (70.8)	18.6 (8.0, NE)	7	2 (28.6)	5 (71.4)	NE (0.1, NE)	0.5061 (0.0962, 2.6613) 0.4213	0.4126	
No	347	120 (34.6)	227 (65.4)	18.0 (12.3, NE)	165	34 (20.6)	131 (79.4)	NE (NE, NE)	1.1814 (0.8026, 1.7390) 0.3981	0.3989	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.5237
Normal Function	201	66 (32.8)	135 (67.2)	18.6 (12.4, NE)	80	12 (15.0)	68 (85.0)	NE (NE, NE)	1.5202 (0.8151, 2.8351) 0.1878	0.1850	
Mild Impairment	123	42 (34.1)	81 (65.9)	NE (9.7, NE)	65	14 (21.5)	51 (78.5)	NE (7.1, NE)	1.0366 (0.5576, 1.9270) 0.9095	0.9085	
Moderate Impairment	41	15 (36.6)	26 (63.4)	12.3 (11.5, NE)	23	8 (34.8)	15 (65.2)	NE (3.1, NE)	0.9358 (0.3955, 2.2145) 0.8801	0.8800	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.9087
Normal Function	170	66 (38.8)	104 (61.2)	12.8 (11.5, NE)	88	21 (23.9)	67 (76.1)	NE (NE, NE)	1.1557 (0.7031, 1.8997) 0.5681	0.5680	
Mild Impairment	194	56 (28.9)	138 (71.1)	18.6 (12.7, NE)	82	13 (15.9)	69 (84.1)	NE (NE, NE)	1.1862 (0.6394, 2.2006) 0.5881	0.5880	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1689
Yes	331	114 (34.4)	217 (65.6)	18.0 (12.3, NE)	146	28 (19.2)	118 (80.8)	NE (NE, NE)	1.2602 (0.8284, 1.9170) 0.2799	0.2790	
No	40	13 (32.5)	27 (67.5)	NE (5.8, NE)	26	8 (30.8)	18 (69.2)	NE (2.9, NE)	0.6220 (0.2484, 1.5573) 0.3106	0.3068	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.1796
Positive	329	106 (32.2)	223 (67.8)	18.6 (12.7, NE)	152	26 (17.1)	126 (82.9)	NE (NE, NE)	1.2663 (0.8191, 1.9576) 0.2882	0.2872	
Negative	42	21 (50.0)	21 (50.0)	6.5 (3.0, NE)	20	10 (50.0)	10 (50.0)	2.9 (1.2, NE)	0.7709 (0.3548, 1.6749) 0.5110	0.5058	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.2759
Positive	331	107 (32.3)	224 (67.7)	18.6 (12.7, NE)	155	28 (18.1)	127 (81.9)	NE (NE, NE)	1.2059 (0.7900, 1.8407)	0.3856	0.3853
Negative	40	20 (50.0)	20 (50.0)	6.5 (2.3, NE)	17	8 (47.1)	9 (52.9)	3.7 (1.0, NE)	0.7860 (0.3371, 1.8327)	0.5772	0.5735

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Urinary tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.6060
HER2 IHC 1+	214	16 (7.5)	198 (92.5)	NE (NE, NE)	100	4 (4.0)	96 (96.0)	NE (NE, NE)	1.2700 (0.4176, 3.8620) 0.6736	0.6732	
HER2 IHC 2+/ISH Negative	157	13 (8.3)	144 (91.7)	NE (NE, NE)	72	2 (2.8)	70 (97.2)	NE (NE, NE)	2.1373 (0.4765, 9.5860) 0.3212	0.3096	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Infections and infestations; PT: Urinary tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.9331
1	220	16 (7.3)	204 (92.7)	NE (NE, NE)	94	3 (3.2)	91 (96.8)	NE (NE, NE)	1.5285 (0.4392, 5.3193) 0.5049	0.5014	
>=2	150	13 (8.7)	137 (91.3)	NE (NE, NE)	78	3 (3.8)	75 (96.2)	NE (NE, NE)	1.6574 (0.4646, 5.9124) 0.4362	0.4315	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Urinary tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.5535
Yes	233	17 (7.3)	216 (92.7)	NE (NE, NE)	112	3 (2.7)	109 (97.3)	NE (NE, NE)	1.8219 (0.5236, 6.3395) 0.3457	0.3385	
No	98	6 (6.1)	92 (93.9)	NE (NE, NE)	43	2 (4.7)	41 (95.3)	NE (NE, NE)	0.8878 (0.1767, 4.4615) 0.8852	0.8851	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Infections and infestations; PT: Urinary tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3301
<65	289	21 (7.3)	268 (92.7)	NE (NE, NE)	126	5 (4.0)	121 (96.0)	NE (NE, NE)	1.2244 (0.4543, 3.2997) 0.6890	0.6885	
>=65	82	8 (9.8)	74 (90.2)	NE (NE, NE)	46	1 (2.2)	45 (97.8)	NE (NE, NE)	3.4564 (0.4289, 27.8552) 0.2441	0.2151	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Infections and infestations; PT: Urinary tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2308
<75	357	27 (7.6)	330 (92.4)	NE (NE, NE)	163	6 (3.7)	157 (96.3)	NE (NE, NE)	1.3943 (0.5680, 3.4230) 0.4682	0.4660	
>=75	14	2 (14.3)	12 (85.7)	NE (5.5, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9979	0.2692	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Infections and infestations; PT: Urinary tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.6512
White	175	17 (9.7)	158 (90.3)	NE (NE, NE)	85	3 (3.5)	82 (96.5)	NE (NE, NE)	1.6990 (0.4889, 5.9039) 0.4042	0.3988	
Non-White	196	12 (6.1)	184 (93.9)	NE (NE, NE)	86	3 (3.5)	83 (96.5)	NE (NE, NE)	1.3833 (0.3865, 4.9507) 0.6179	0.6166	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Urinary tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.1250
Asia	147	6 (4.1)	141 (95.9)	NE (NE, NE)	63	2 (3.2)	61 (96.8)	NE (NE, NE)	0.9566 (0.1904, 4.8060) 0.9570	0.9575	
North America	58	9 (15.5)	49 (84.5)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9941	0.0846	
Europe + Israel	166	14 (8.4)	152 (91.6)	NE (NE, NE)	81	4 (4.9)	77 (95.1)	NE (NE, NE)	1.1363 (0.3664, 3.5242) 0.8248	0.8253	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Infections and infestations; PT: Urinary tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.5718
0	199	16 (8.0)	183 (92.0)	NE (NE, NE)	95	4 (4.2)	91 (95.8)	NE (NE, NE)	1.0426 (0.3434, 3.1653) 0.9413	0.9406	
1	172	13 (7.6)	159 (92.4)	NE (NE, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	2.6236 (0.5883, 11.7001) 0.2060	0.1892	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Infections and infestations; PT: Urinary tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.8028
0	60	9 (15.0)	51 (85.0)	NE (14.7, NE)	31	1 (3.2)	30 (96.8)	NE (NE, NE)	3.0085 (0.3759, 24.0781) 0.2993	0.2758	
1	107	9 (8.4)	98 (91.6)	NE (NE, NE)	48	2 (4.2)	46 (95.8)	NE (NE, NE)	1.6651 (0.3573, 7.7595) 0.5161	0.5117	
2	114	7 (6.1)	107 (93.9)	NE (NE, NE)	50	2 (4.0)	48 (96.0)	NE (NE, NE)	1.0155 (0.2007, 5.1369) 0.9852	0.9851	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Infections and infestations; PT: Urinary tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	4 (4.4)	86 (95.6)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	1.2540 (0.1336, 11.7683) 0.8430	0.8426	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Urinary tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.6235
PD	173	12 (6.9)	161 (93.1)	NE (NE, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	1.1838 (0.3281, 4.2707)	0.7963	
PR	48	2 (4.2)	46 (95.8)	NE (NE, NE)	21	1 (4.8)	20 (95.2)	NE (NE, NE)	0.6628 (0.0589, 7.4542)	0.7375	
SD	82	9 (11.0)	73 (89.0)	NE (NE, NE)	54	2 (3.7)	52 (96.3)	NE (NE, NE)	2.0989 (0.4465, 9.8670)	0.3373	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:37; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_AESOCPT10PAT\_2\_SAS.rf



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SOC: Infections and infestations; PT: Urinary tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.4427
Yes	37	2 (5.4)	35 (94.6)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9974	0.4722	
No	334	27 (8.1)	307 (91.9)	NE (NE, NE)	159	6 (3.8)	153 (96.2)	NE (NE, NE)	1.4670 (0.5984, 3.5967) 0.4023	0.3992	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Urinary tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.5808
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9982	0.6374	
No	347	28 (8.1)	319 (91.9)	NE (NE, NE)	165	6 (3.6)	159 (96.4)	NE (NE, NE)	1.5178 (0.6210, 3.7096) 0.3601	0.3563	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Infections and infestations; PT: Urinary tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0687
Normal Function	201	13 (6.5)	188 (93.5)	NE (NE, NE)	80	0	80 (100)	NE (NE, NE)	NE (NE, NE) 0.9935	0.0669	
Mild Impairment	123	12 (9.8)	111 (90.2)	NE (NE, NE)	65	4 (6.2)	61 (93.8)	NE (NE, NE)	1.0735 (0.3397, 3.3921) 0.9038	0.9041	
Moderate Impairment	41	3 (7.3)	38 (92.7)	NE (NE, NE)	23	2 (8.7)	21 (91.3)	NE (NE, NE)	0.7190 (0.1194, 4.3297) 0.7188	0.7176	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Urinary tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.0427
Normal Function	170	14 (8.2)	156 (91.8)	NE (NE, NE)	88	1 (1.1)	87 (98.9)	NE (NE, NE)	4.9348 (0.6433, 37.8526) 0.1246	0.0891	
Mild Impairment	194	12 (6.2)	182 (93.8)	NE (NE, NE)	82	5 (6.1)	77 (93.9)	NE (NE, NE)	0.6381 (0.2183, 1.8651) 0.4117	0.4087	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Urinary tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.0885
Yes	331	23 (6.9)	308 (93.1)	NE (NE, NE)	146	6 (4.1)	140 (95.9)	NE (NE, NE)	1.2708 (0.5124, 3.1520) 0.6050	0.6043	
No	40	6 (15.0)	34 (85.0)	NE (14.7, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9960	0.2585	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Urinary tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.6173
Positive	329	22 (6.7)	307 (93.3)	NE (NE, NE)	152	5 (3.3)	147 (96.7)	NE (NE, NE)	1.3315 (0.4972, 3.5658)	0.5673	
Negative	42	7 (16.7)	35 (83.3)	NE (NE, NE)	20	1 (5.0)	19 (95.0)	NE (NE, NE)	2.8850 (0.3511, 23.7031)	0.3022	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Infections and infestations; PT: Urinary tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.7356
Positive	331	22 (6.6)	309 (93.4)	NE (NE, NE)	155	5 (3.2)	150 (96.8)	NE (NE, NE)	1.3568 (0.5064, 3.6353)	0.5422	
Negative	40	7 (17.5)	33 (82.5)	NE (NE, NE)	17	1 (5.9)	16 (94.1)	NE (NE, NE)	2.4244 (0.2941, 19.9838)	0.3957	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Infections and infestations; PT: Upper respiratory tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.1007
HER2 IHC 1+	214	12 (5.6)	202 (94.4)	NE (NE, NE)	100	0	100 (100)	NE (NE, NE)	NE (NE, NE) 0.9930	0.0380	
HER2 IHC 2+/ISH Negative	157	4 (2.5)	153 (97.5)	NE (NE, NE)	72	1 (1.4)	71 (98.6)	NE (NE, NE)	1.1252 (0.1202, 10.5294) 0.9177	0.9176	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Upper respiratory tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.2647
1	220	8 (3.6)	212 (96.4)	NE (NE, NE)	94	0	94 (100)	NE (NE, NE)	NE (NE, NE) 0.9945	0.1126	
>=2	150	8 (5.3)	142 (94.7)	NE (NE, NE)	78	1 (1.3)	77 (98.7)	NE (NE, NE)	2.9141 (0.3566, 23.8172) 0.3184	0.2966	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Infections and infestations; PT: Upper respiratory tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											1.0000
Yes	233	10 (4.3)	223 (95.7)	NE (NE, NE)	112	0	112 (100)	NE (NE, NE)	NE (NE, NE) 0.9935	0.0530	
No	98	5 (5.1)	93 (94.9)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9955	0.1861	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Upper respiratory tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1099
<65	289	13 (4.5)	276 (95.5)	NE (NE, NE)	126	0	126 (100)	NE (NE, NE)	NE (NE, NE) 0.9930	0.0402	
>=65	82	3 (3.7)	79 (96.3)	NE (NE, NE)	46	1 (2.2)	45 (97.8)	NE (NE, NE)	1.1944 (0.1224, 11.6600) 0.8785	0.8784	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Upper respiratory tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0500
<75	357	15 (4.2)	342 (95.8)	NE (NE, NE)	163	0	163 (100)	NE (NE, NE)	NE (NE, NE) 0.9923	0.0232	
>=75	14	1 (7.1)	13 (92.9)	NE (6.3, NE)	9	1 (11.1)	8 (88.9)	NE (3.7, NE)	0.5318 (0.0329, 8.5980) 0.6565	0.6513	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Upper respiratory tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.1754
White	175	6 (3.4)	169 (96.6)	NE (NE, NE)	85	1 (1.2)	84 (98.8)	NE (NE, NE)	1.3698 (0.1555, 12.0626) 0.7768	0.7758	
Non-White	196	10 (5.1)	186 (94.9)	NE (NE, NE)	86	0	86 (100)	NE (NE, NE)	NE (NE, NE) 0.9933	0.0467	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Upper respiratory tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.2934
Asia	147	10 (6.8)	137 (93.2)	NE (NE, NE)	63	0	63 (100)	NE (NE, NE)	NE (NE, NE) 0.9934	0.0497	
North America	58	2 (3.4)	56 (96.6)	NE (18.0, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.5734	
Europe + Israel	166	4 (2.4)	162 (97.6)	NE (NE, NE)	81	1 (1.2)	80 (98.8)	NE (NE, NE)	1.1393 (0.1229, 10.5646) 0.9086	0.9085	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Upper respiratory tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.0772
0	199	13 (6.5)	186 (93.5)	NE (NE, NE)	95	0	95 (100)	NE (NE, NE)	NE (NE, NE) 0.9928	0.0315	
1	172	3 (1.7)	169 (98.3)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	0.8211 (0.0824, 8.1834) 0.8666	0.8664	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Upper respiratory tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.6417
0	60	6 (10.0)	54 (90.0)	NE (NE, NE)	31	1 (3.2)	30 (96.8)	NE (NE, NE)	2.3016 (0.2698, 19.6318) 0.4459	0.4333	
1	107	4 (3.7)	103 (96.3)	NE (NE, NE)	48	0	48 (100)	NE (NE, NE)	NE (NE, NE) 0.9957	0.2051	
2	114	3 (2.6)	111 (97.4)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	NE (NE, NE) 0.9966	0.3300	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Upper respiratory tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	3 (3.3)	87 (96.7)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9970	0.4016	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Upper respiratory tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.6449
PD	173	8 (4.6)	165 (95.4)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	2.1262 (0.2555, 17.6924)	0.4754	
PR	48	2 (4.2)	46 (95.8)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	NE (NE, NE) 0.9972	0.4297	
SD	82	2 (2.4)	80 (97.6)	NE (NE, NE)	54	0	54 (100)	NE (NE, NE)	NE (NE, NE) 0.9967	0.2908	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Upper respiratory tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.7680
Yes	37	1 (2.7)	36 (97.3)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.7518	
No	334	15 (4.5)	319 (95.5)	NE (NE, NE)	159	1 (0.6)	158 (99.4)	NE (NE, NE)	5.4208 (0.7096, 41.4091) 0.1032	0.0677	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.8.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Infections and infestations; PT: Upper respiratory tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.7653
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9985	0.6949	
No	347	15 (4.3)	332 (95.7)	NE (NE, NE)	165	1 (0.6)	164 (99.4)	NE (NE, NE)	5.3505 (0.7001, 40.8891) 0.1060	0.0704	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Upper respiratory tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0332
Normal Function	201	7 (3.5)	194 (96.5)	NE (NE, NE)	80	0	80 (100)	NE (NE, NE)	NE (NE, NE) 0.9949	0.1431	
Mild Impairment	123	8 (6.5)	115 (93.5)	NE (NE, NE)	65	0	65 (100)	NE (NE, NE)	NE (NE, NE) 0.9945	0.1024	
Moderate Impairment	41	0	41 (100)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	0.0000 (0.0000, ) 0.9977	0.1510	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.8.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Infections and infestations; PT: Upper respiratory tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.2436
Normal Function	170	7 (4.1)	163 (95.9)	NE (NE, NE)	88	1 (1.1)	87 (98.9)	NE (NE, NE)	2.9304 (0.3587, 23.9420) 0.3158	0.2930	
Mild Impairment	194	9 (4.6)	185 (95.4)	NE (NE, NE)	82	0	82 (100)	NE (NE, NE)	NE (NE, NE) 0.9946	0.1167	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Upper respiratory tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.0922
Yes	331	13 (3.9)	318 (96.1)	NE (NE, NE)	146	0	146 (100)	NE (NE, NE)	NE (NE, NE) 0.9929	0.0393	
No	40	3 (7.5)	37 (92.5)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	1.1276 (0.1084, 11.7245) 0.9199	0.9199	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Upper respiratory tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.0270
Positive	329	15 (4.6)	314 (95.4)	NE (NE, NE)	152	0	152 (100)	NE (NE, NE)	NE (NE, NE) 0.9922	0.0214	
Negative	42	1 (2.4)	41 (97.6)	NE (NE, NE)	20	1 (5.0)	19 (95.0)	NE (3.7, NE)	0.1165 (0.0058, 2.3260) 0.1593	0.1045	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Upper respiratory tract infection

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.0227
Positive	331	15 (4.5)	316 (95.5)	NE (NE, NE)	155	0	155 (100)	NE (NE, NE)	NE (NE, NE) 0.9922	0.0204	
Negative	40	1 (2.5)	39 (97.5)	NE (NE, NE)	17	1 (5.9)	16 (94.1)	NE (3.7, NE)	0.1026 (0.0055, 1.9168) 0.1274	0.0696	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Pneumonia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.8385
HER2 IHC 1+	214	6 (2.8)	208 (97.2)	NE (NE, NE)	100	1 (1.0)	99 (99.0)	NE (NE, NE)	1.9836 (0.2347, 16.7650) 0.5294	0.5216	
HER2 IHC 2+/ISH Negative	157	9 (5.7)	148 (94.3)	NE (NE, NE)	72	2 (2.8)	70 (97.2)	NE (NE, NE)	1.0585 (0.2225, 5.0342) 0.9431	0.9431	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Pneumonia

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting									0.8566
1	220	6 (2.7)	214 (97.3)	94	1 (1.1)	93 (98.9)	NE (NE, NE)	1.6443 (0.1948, 13.8818) 0.6477	0.6444
>=2	150	9 (6.0)	141 (94.0)	78	2 (2.6)	76 (97.4)	NE (NE, NE)	1.2299 (0.2561, 5.9068) 0.7960	0.7957

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Infections and infestations; PT: Pneumonia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.2224
Yes	233	6 (2.6)	227 (97.4)	NE (NE, NE)	112	1 (0.9)	111 (99.1)	NE (NE, NE)	1.5408 (0.1785, 13.3021) 0.6943	0.6921	
No	98	6 (6.1)	92 (93.9)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9957	0.2374	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Infections and infestations; PT: Pneumonia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1826
<65	289	12 (4.2)	277 (95.8)	NE (NE, NE)	126	3 (2.4)	123 (97.6)	NE (NE, NE)	0.9769 (0.2692, 3.5454) 0.9717	0.9718	
>=65	82	3 (3.7)	79 (96.3)	NE (NE, NE)	46	0	46 (100)	NE (NE, NE)	NE (NE, NE) 0.9966	0.3301	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Pneumonia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9999
<75	357	15 (4.2)	342 (95.8)	NE (NE, NE)	163	3 (1.8)	160 (98.2)	NE (NE, NE)	1.2805 (0.3623, 4.5257) 0.7011	0.7003	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Pneumonia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.0271
White	175	9 (5.1)	166 (94.9)	NE (NE, NE)	85	0	85 (100)	NE (NE, NE)	NE (NE, NE) 0.9946	0.1376	
Non-White	196	6 (3.1)	190 (96.9)	NE (NE, NE)	86	3 (3.5)	83 (96.5)	NE (NE, NE)	0.5488 (0.1309, 2.3004) 0.4118	0.4055	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Pneumonia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.2019
Asia	147	5 (3.4)	142 (96.6)	NE (NE, NE)	63	2 (3.2)	61 (96.8)	NE (NE, NE)	0.5638 (0.1034, 3.0731) 0.5077	0.5025	
North America	58	4 (6.9)	54 (93.1)	NE (NE, NE)	28	1 (3.6)	27 (96.4)	NE (NE, NE)	1.5164 (0.1675, 13.7269) 0.7111	0.7089	
Europe + Israel	166	6 (3.6)	160 (96.4)	NE (NE, NE)	81	0	81 (100)	NE (NE, NE)	NE (NE, NE) 0.9958	0.2490	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Pneumonia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.2774
0	199	5 (2.5)	194 (97.5)	NE (NE, NE)	95	2 (2.1)	93 (97.9)	NE (NE, NE)	0.8025 (0.1526, 4.2211) 0.7951	0.7947	
1	172	10 (5.8)	162 (94.2)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	2.2680 (0.2813, 18.2873) 0.4419	0.4298	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Pneumonia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.5733
0	60	5 (8.3)	55 (91.7)	NE (NE, NE)	31	2 (6.5)	29 (93.5)	NE (NE, NE)	0.7188 (0.1365, 3.7870) 0.6970	0.6959	
1	107	5 (4.7)	102 (95.3)	NE (NE, NE)	48	1 (2.1)	47 (97.9)	NE (NE, NE)	1.9557 (0.2268, 16.8656) 0.5417	0.5343	
2	114	4 (3.5)	110 (96.5)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	NE (NE, NE) 0.9959	0.4849	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Pneumonia

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	1 (1.1)	89 (98.9) NE (NE, NE)	43	0	43 (100) NE (NE, NE)	NE (NE, NE) 0.9986	0.8231	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Pneumonia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.4647
PD	173	7 (4.0)	166 (96.0)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	1.7440 (0.2083, 14.6019)	0.6036	
PR	48	1 (2.1)	47 (97.9)	NE (15.2, NE)	21	0	21 (100)	NE (NE, NE)	0.6080 (0.0000, )	1.0000	
SD	82	2 (2.4)	80 (97.6)	NE (NE, NE)	54	2 (3.7)	52 (96.3)	NE (NE, NE)	0.5826 (0.0816, 4.1620)	0.5858	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Pneumonia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.1789
Yes	37	1 (2.7)	36 (97.3)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	0.2265 (0.0134, 3.8135)	0.3026	0.2626
No	334	14 (4.2)	320 (95.8)	NE (NE, NE)	159	2 (1.3)	157 (98.7)	NE (NE, NE)	1.8739 (0.4172, 8.4172)	0.4126	0.4053

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Pneumonia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0403
Yes	24	0	24 (100)	NE (NE, NE)	7	1 (14.3)	6 (85.7)	NE (0.8, NE)	0.0000 (0.0000, ) 0.9982	0.0699	
No	347	15 (4.3)	332 (95.7)	NE (NE, NE)	165	2 (1.2)	163 (98.8)	NE (NE, NE)	1.9693 (0.4419, 8.7769) 0.3741	0.3654	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Pneumonia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.3036
Normal Function	201	7 (3.5)	194 (96.5)	NE (NE, NE)	80	2 (2.5)	78 (97.5)	NE (NE, NE)	0.8881 (0.1783, 4.4224) 0.8848	0.8847	
Mild Impairment	123	5 (4.1)	118 (95.9)	NE (NE, NE)	65	0	65 (100)	NE (NE, NE)	NE (NE, NE) 0.9960	0.2510	
Moderate Impairment	41	3 (7.3)	38 (92.7)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	1.3866 (0.1441, 13.3440) 0.7772	0.7762	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Pneumonia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1303
Normal Function	170	9 (5.3)	161 (94.7)	NE (NE, NE)	88	3 (3.4)	85 (96.6)	NE (NE, NE)	0.8513 (0.2246, 3.2264) 0.8128	0.8126	
Mild Impairment	194	6 (3.1)	188 (96.9)	NE (NE, NE)	82	0	82 (100)	NE (NE, NE)	NE (NE, NE) 0.9955	0.1983	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Pneumonia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.0638
Yes	331	13 (3.9)	318 (96.1)	NE (NE, NE)	146	1 (0.7)	145 (99.3)	NE (NE, NE)	3.2993 (0.4250, 25.6112) 0.2536	0.2269	
No	40	2 (5.0)	38 (95.0)	NE (NE, NE)	26	2 (7.7)	24 (92.3)	NE (NE, NE)	0.3782 (0.0518, 2.7604) 0.3377	0.3203	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Pneumonia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.0013
Positive	329	13 (4.0)	316 (96.0)	NE (NE, NE)	152	0	152 (100)	NE (NE, NE)	NE (NE, NE) 0.9902	0.0794	
Negative	42	2 (4.8)	40 (95.2)	NE (NE, NE)	20	3 (15.0)	17 (85.0)	NE (NE, NE)	0.2560 (0.0416, 1.5739) 0.1414	0.1144	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Pneumonia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.0362
Positive	331	13 (3.9)	318 (96.1)	NE (NE, NE)	155	1 (0.6)	154 (99.4)	NE (NE, NE)	3.2681 (0.4208, 25.3791) 0.2575	0.2311	
Negative	40	2 (5.0)	38 (95.0)	NE (NE, NE)	17	2 (11.8)	15 (88.2)	NE (2.8, NE)	0.3214 (0.0436, 2.3695) 0.2654	0.2422	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Nasopharyngitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.9949
HER2 IHC 1+	214	7 (3.3)	207 (96.7)	NE (NE, NE)	100	1 (1.0)	99 (99.0)	NE (NE, NE)	1.7263 (0.2037, 14.6283) 0.6166	0.6124	
HER2 IHC 2+/ISH Negative	157	7 (4.5)	150 (95.5)	NE (NE, NE)	72	1 (1.4)	71 (98.6)	NE (NE, NE)	1.9964 (0.2397, 16.6297) 0.5227	0.5148	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Infections and infestations; PT: Nasopharyngitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.3205
1	220	11 (5.0)	209 (95.0)	NE (NE, NE)	94	2 (2.1)	92 (97.9)	NE (NE, NE)	1.5208 (0.3304, 6.9996) 0.5904	0.5878	
>=2	150	3 (2.0)	147 (98.0)	NE (NE, NE)	78	0	78 (100)	NE (NE, NE)	NE (NE, NE) 0.9970	0.4001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Infections and infestations; PT: Nasopharyngitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.6052
Yes	233	9 (3.9)	224 (96.1)	NE (NE, NE)	112	1 (0.9)	111 (99.1)	NE (NE, NE)	2.7560 (0.3423, 22.1911) 0.3408	0.3208	
No	98	4 (4.1)	94 (95.9)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	1.0438 (0.1129, 9.6522) 0.9699	0.9695	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Infections and infestations; PT: Nasopharyngitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6168
<65	289	6 (2.1)	283 (97.9)	NE (NE, NE)	126	1 (0.8)	125 (99.2)	NE (NE, NE)	1.4419 (0.1650, 12.5971) 0.7407	0.7392	
>=65	82	8 (9.8)	74 (90.2)	NE (NE, NE)	46	1 (2.2)	45 (97.8)	NE (NE, NE)	3.1995 (0.3934, 26.0204) 0.2768	0.2510	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0853
<75	357	10 (2.8)	347 (97.2)	NE (NE, NE)	163	2 (1.2)	161 (98.8)	NE (NE, NE)	1.1377 (0.2393, 5.4085) 0.8712	0.8711	
>=75	14	4 (28.6)	10 (71.4)	NE (3.3, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9969	0.0935	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.4882
White	175	3 (1.7)	172 (98.3)	NE (NE, NE)	85	0	85 (100)	NE (NE, NE)	NE (NE, NE) 0.9966	0.3114	
Non-White	196	11 (5.6)	185 (94.4)	NE (NE, NE)	86	1 (1.2)	85 (98.8)	NE (NE, NE)	2.6172 (0.3324, 20.6061) 0.3608	0.3428	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.8058
Asia	147	9 (6.1)	138 (93.9)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (NE, NE)	2.1123 (0.2628, 16.9778) 0.4819	0.4720	
North America	58	1 (1.7)	57 (98.3)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9978	0.4951	
Europe + Israel	166	4 (2.4)	162 (97.6)	NE (NE, NE)	81	1 (1.2)	80 (98.8)	NE (NE, NE)	1.1167 (0.1176, 10.6002) 0.9234	0.9234	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Nasopharyngitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.4570
0	199	12 (6.0)	187 (94.0)	NE (NE, NE)	95	2 (2.1)	93 (97.9)	NE (NE, NE)	1.6785 (0.3674, 7.6682) 0.5040	0.4995	
1	172	2 (1.2)	170 (98.8)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE) 0.9973	0.4443	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Nasopharyngitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.2544
0	60	1 (1.7)	59 (98.3)	NE (NE, NE)	31	1 (3.2)	30 (96.8)	NE (NE, NE)	0.2887 (0.0160, 5.1944) 0.3994	0.3750	
1	107	5 (4.7)	102 (95.3)	NE (NE, NE)	48	0	48 (100)	NE (NE, NE)	NE (NE, NE) 0.9955	0.1973	
2	114	3 (2.6)	111 (97.4)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	NE (NE, NE) 0.9961	0.4792	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Nasopharyngitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	5 (5.6)	85 (94.4)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	1.3183 (0.1485, 11.7056) 0.8041	0.8034	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Nasopharyngitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.7734
PD	173	6 (3.5)	167 (96.5)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	1.7654 (0.2043, 15.2536)	0.6008	
PR	48	2 (4.2)	46 (95.8)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	0.6054 (NE, NE)	0.4758	
SD	82	4 (4.9)	78 (95.1)	NE (NE, NE)	54	1 (1.9)	53 (98.1)	NE (NE, NE)	1.6245 (0.1790, 14.7423)	0.6633	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Infections and infestations; PT: Nasopharyngitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.5099
Yes	37	2 (5.4)	35 (94.6)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9974	0.4760	
No	334	12 (3.6)	322 (96.4)	NE (NE, NE)	159	2 (1.3)	157 (98.7)	NE (NE, NE)	1.5778 (0.3433, 7.2521) 0.5578	0.5546	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Nasopharyngitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.6374
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9981	0.5892	
No	347	13 (3.7)	334 (96.3)	NE (NE, NE)	165	2 (1.2)	163 (98.8)	NE (NE, NE)	1.7051 (0.3754, 7.7453) 0.4896	0.4847	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Nasopharyngitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.4300
Normal Function	201	5 (2.5)	196 (97.5)	NE (NE, NE)	80	1 (1.3)	79 (98.8)	NE (NE, NE)	0.8954 (0.0940, 8.5266)	0.9234	
Mild Impairment	123	4 (3.3)	119 (96.7)	NE (NE, NE)	65	1 (1.5)	64 (98.5)	NE (NE, NE)	1.2823 (0.1404, 11.7151)	0.8252	
Moderate Impairment	41	3 (7.3)	38 (92.7)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE)	0.2292	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Nasopharyngitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1378
Normal Function	170	6 (3.5)	164 (96.5)	NE (NE, NE)	88	2 (2.3)	86 (97.7)	NE (NE, NE)	0.9494 (0.1836, 4.9089) 0.9506	0.9506	
Mild Impairment	194	6 (3.1)	188 (96.9)	NE (NE, NE)	82	0	82 (100)	NE (NE, NE)	NE (NE, NE) 0.9935	0.2474	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Nasopharyngitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.5924
Yes	331	13 (3.9)	318 (96.1)	NE (NE, NE)	146	2 (1.4)	144 (98.6)	NE (NE, NE)	1.6771 (0.3710, 7.5804) 0.5017	0.4971	
No	40	1 (2.5)	39 (97.5)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9976	0.4201	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Nasopharyngitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.6043
Positive	329	13 (4.0)	316 (96.0)	NE (NE, NE)	152	2 (1.3)	150 (98.7)	NE (NE, NE)	1.8337 (0.4053, 8.2959) 0.4311	0.4243	
Negative	42	1 (2.4)	41 (97.6)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.7456	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:37; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_AESOCPT10PAT\_2\_SAS.rf

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SOC: Infections and infestations; PT: Nasopharyngitis

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.6335
Positive	331	13 (3.9)	318 (96.1)	NE (NE, NE)	155	2 (1.3)	153 (98.7)	NE (NE, NE)	1.8611 (0.4112, 8.4232)	0.4129	
Negative	40	1 (2.5)	39 (97.5)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	0.4200 (NE, NE) 0.9980	0.7456	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:37; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_AESOCPT10PAT\_2\_SAS.rtf

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SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
HER2 status											
HER2 IHC 1+	214	28 (13.1)	186 (86.9)	NE (NE, NE)	100	17 (17.0)	83 (83.0)	NE (11.3, NE)	0.4233 (0.2257, 0.7939) 0.0074	0.0059	0.0020
HER2 IHC 2+/ISH Negative	157	32 (20.4)	125 (79.6)	NE (NE, NE)	72	4 (5.6)	68 (94.4)	NE (9.9, NE)	2.8684 (1.0064, 8.1756) 0.0486	0.0393	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Run date: 13SEP2022 – 17:37; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_AESOCPT10PAT\_2\_SAS.rtf

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SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.1907
1	220	33 (15.0)	187 (85.0)	NE (NE, NE)	94	14 (14.9)	80 (85.1)	NE (9.9, NE)	0.5918 (0.3104, 1.1284) 0.1111	0.1071	
>=2	150	27 (18.0)	123 (82.0)	NE (NE, NE)	78	7 (9.0)	71 (91.0)	NE (NE, NE)	1.5252 (0.6569, 3.5415) 0.3260	0.3224	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.8881
Yes	233	42 (18.0)	191 (82.0)	NE (NE, NE)	112	16 (14.3)	96 (85.7)	NE (9.9, NE)	0.7609 (0.4184, 1.3838) 0.3705	0.3678	
No	98	11 (11.2)	87 (88.8)	NE (NE, NE)	43	4 (9.3)	39 (90.7)	NE (11.3, NE)	0.8783 (0.2758, 2.7968) 0.8262	0.8261	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2683
<65	289	39 (13.5)	250 (86.5)	NE (NE, NE)	126	14 (11.1)	112 (88.9)	NE (9.9, NE)	0.7465 (0.3977, 1.4012) 0.3628	0.3608	
>=65	82	21 (25.6)	61 (74.4)	NE (NE, NE)	46	7 (15.2)	39 (84.8)	NE (11.3, NE)	1.3559 (0.5722, 3.2132) 0.4891	0.4870	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3362
<75	357	55 (15.4)	302 (84.6)	NE (NE, NE)	163	19 (11.7)	144 (88.3)	NE (9.9, NE)	0.8576 (0.5015, 1.4668) 0.5749	0.5737	
>=75	14	5 (35.7)	9 (64.3)	6.2 (3.9, NE)	9	2 (22.2)	7 (77.8)	NE (2.1, NE)	1.9361 (0.3680, 10.1858) 0.4355	0.4277	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.4975
White	175	38 (21.7)	137 (78.3)	NE (NE, NE)	85	12 (14.1)	73 (85.9)	NE (NE, NE)	1.0062 (0.5170, 1.9584) 0.9855	0.9871	
Non-White	196	22 (11.2)	174 (88.8)	NE (NE, NE)	86	9 (10.5)	77 (89.5)	NE (9.9, NE)	0.6770 (0.3050, 1.5025) 0.3376	0.3358	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.0212
Asia	147	17 (11.6)	130 (88.4)	NE (NE, NE)	63	3 (4.8)	60 (95.2)	NE (9.9, NE)	1.4080 (0.4028, 4.9225) 0.5920	0.5900	
North America	58	10 (17.2)	48 (82.8)	NE (NE, NE)	28	9 (32.1)	19 (67.9)	NE (2.1, NE)	0.3456 (0.1366, 0.8743) 0.0248	0.0192	
Europe + Israel	166	33 (19.9)	133 (80.1)	NE (NE, NE)	81	9 (11.1)	72 (88.9)	NE (NE, NE)	1.2122 (0.5712, 2.5725) 0.6163	0.6164	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.9236
0	199	34 (17.1)	165 (82.9)	NE (NE, NE)	95	12 (12.6)	83 (87.4)	NE (9.9, NE)	0.8966 (0.4582, 1.7544) 0.7500	0.7482	
1	172	26 (15.1)	146 (84.9)	NE (NE, NE)	77	9 (11.7)	68 (88.3)	NE (11.3, NE)	0.8102 (0.3695, 1.7766) 0.5994	0.5985	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)									0.8006
0	60 (11.7)	7 (1.7)	53 (88.3) (NE, NE)	31 (12.9)	4 (1.9)	27 (87.1) (3.9, NE)	0.5438 (0.1550, 1.9082) 0.3415	0.3345	
1	107 (15.0)	16 (15.0)	91 (85.0) (NE, NE)	48 (14.6)	7 (14.6)	41 (85.4) (11.3, NE)	0.7109 (0.2892, 1.7471) 0.4570	0.4551	
2	114 (16.7)	19 (16.7)	95 (83.3) (NE, NE)	50 (12.0)	6 (12.0)	44 (88.0) (NE, NE)	0.9339 (0.3644, 2.3938) 0.8868	0.8864	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 (20.0)	72 (80.0)	NE (NE, NE)	43 (9.3)	39 (90.7)	NE (9.9, NE)	1.4815 (0.4875, 4.5022) 0.4883	0.4877	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.4762
PD	173	28 (16.2)	145 (83.8)	NE (NE, NE)	77	8 (10.4)	69 (89.6)	NE (NE, NE)	1.0765 (0.4813, 2.4082)	0.8575	0.8576
PR	48	11 (22.9)	37 (77.1)	NE (14.0, NE)	21	2 (9.5)	19 (90.5)	NE (4.8, NE)	1.5683 (0.3401, 7.2317)	0.5639	0.5607
SD	82	12 (14.6)	70 (85.4)	NE (NE, NE)	54	9 (16.7)	45 (83.3)	NE (9.9, NE)	0.4990 (0.2043, 1.2188)	0.1271	0.1208

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.1159
Yes	37	5 (13.5)	32 (86.5)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9961	0.2778	
No	334	55 (16.5)	279 (83.5)	NE (NE, NE)	159	21 (13.2)	138 (86.8)	NE (11.3, NE)	0.8124 (0.4849, 1.3611) 0.4301	0.4292	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.9216
Yes	24	4 (16.7)	20 (83.3)	NE (11.1, NE)	7	1 (14.3)	6 (85.7)	NE (3.9, NE)	0.8785 (0.0961, 8.0271) 0.9086	0.9086	
No	347	56 (16.1)	291 (83.9)	NE (NE, NE)	165	20 (12.1)	145 (87.9)	NE (11.3, NE)	0.8672 (0.5138, 1.4636) 0.5935	0.5926	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.7133
Normal Function	201	26 (12.9)	175 (87.1)	NE (NE, NE)	80	8 (10.0)	72 (90.0)	NE (9.9, NE)	0.7624 (0.3349, 1.7354) 0.5179	0.5169	
Mild Impairment	123	25 (20.3)	98 (79.7)	NE (NE, NE)	65	7 (10.8)	58 (89.2)	NE (NE, NE)	1.1304 (0.4764, 2.6824) 0.7810	0.7815	
Moderate Impairment	41	9 (22.0)	32 (78.0)	NE (NE, NE)	23	6 (26.1)	17 (73.9)	NE (3.7, NE)	0.7534 (0.2675, 2.1224) 0.5921	0.5922	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.5151
Normal Function	170	26 (15.3)	144 (84.7)	NE (NE, NE)	88	12 (13.6)	76 (86.4)	NE (NE, NE)	0.7568 (0.3765, 1.5215) 0.4342	0.4323	
Mild Impairment	194	34 (17.5)	160 (82.5)	NE (NE, NE)	82	9 (11.0)	73 (89.0)	11.3 (11.3, NE)	0.9884 (0.4639, 2.1062) 0.9760	0.9755	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1425
Yes	331	56 (16.9)	275 (83.1)	NE (NE, NE)	146	17 (11.6)	129 (88.4)	NE (11.3, NE)	0.9844 (0.5658, 1.7124) 0.9555	0.9546	
No	40	4 (10.0)	36 (90.0)	NE (NE, NE)	26	4 (15.4)	22 (84.6)	NE (3.1, NE)	0.3499 (0.0822, 1.4897) 0.1554	0.1402	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.9614
Positive	329	52 (15.8)	277 (84.2)	NE (NE, NE)	152	18 (11.8)	134 (88.2)	NE (11.3, NE)	0.8730 (0.5045, 1.5109) 0.6275	0.6261	
Negative	42	8 (19.0)	34 (81.0)	NE (9.7, NE)	20	3 (15.0)	17 (85.0)	NE (3.1, NE)	0.7977 (0.2008, 3.1686) 0.7480	0.7476	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Eye disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (derived)											0.4919
Positive	331	54 (16.3)	277 (83.7)	NE (NE, NE)	155	20 (12.9)	135 (87.1)	NE (11.3, NE)	0.8339 (0.4932, 1.4097)	0.4976	0.4962
Negative	40	6 (15.0)	34 (85.0)	NE (9.7, NE)	17	1 (5.9)	16 (94.1)	NE (NE, NE)	1.5311 (0.1739, 13.4822)	0.7011	0.6991

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Vision blurred

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.4409
HER2 IHC 1+	214	8 (3.7)	206 (96.3)	NE (NE, NE)	100	4 (4.0)	96 (96.0)	NE (NE, NE)	0.7535 (0.2232, 2.5441) 0.6485	0.6486	
HER2 IHC 2+/ISH Negative	157	5 (3.2)	152 (96.8)	NE (NE, NE)	72	1 (1.4)	71 (98.6)	NE (NE, NE)	2.1585 (0.2519, 18.4983) 0.4827	0.4719	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Vision blurred

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.8291
1	220	9 (4.1)	211 (95.9)	NE (NE, NE)	94	3 (3.2)	91 (96.8)	NE (NE, NE)	1.1535 (0.3118, 4.2666) 0.8306	0.8309	
>=2	150	4 (2.7)	146 (97.3)	NE (NE, NE)	78	2 (2.6)	76 (97.4)	NE (NE, NE)	0.8700 (0.1542, 4.9091) 0.8746	0.8766	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Vision blurred

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											
Yes	233	9 (3.9)	224 (96.1)	NE (NE, NE)	112	5 (4.5)	107 (95.5)	NE (NE, NE)	0.7702 (0.2574, 2.3045) 0.6405	0.6399	0.2120
No	98	2 (2.0)	96 (98.0)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9970	0.3720	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Vision blurred

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1784
<65	289	11 (3.8)	278 (96.2)	NE (NE, NE)	126	5 (4.0)	121 (96.0)	NE (NE, NE)	0.8079 (0.2778, 2.3500) 0.6954	0.6953	
>=65	82	2 (2.4)	80 (97.6)	NE (NE, NE)	46	0	46 (100)	NE (NE, NE)	NE (NE, NE) 0.9968	0.3056	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Vision blurred

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3056
<75	357	12 (3.4)	345 (96.6)	NE (NE, NE)	163	5 (3.1)	158 (96.9)	NE (NE, NE)	0.9421 (0.3288, 2.6991) 0.9116	0.9119	
>=75	14	1 (7.1)	13 (92.9)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9985	0.4142	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Vision blurred

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.1192
White	175	10 (5.7)	165 (94.3)	NE (NE, NE)	85	2 (2.4)	83 (97.6)	NE (NE, NE)	2.0764 (0.4511, 9.5581) 0.3483	0.3379	
Non-White	196	3 (1.5)	193 (98.5)	NE (NE, NE)	86	3 (3.5)	83 (96.5)	NE (NE, NE)	0.3896 (0.0782, 1.9406) 0.2499	0.2329	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Vision blurred

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.0209
Asia	147	3 (2.0)	144 (98.0)	NE (NE, NE)	63	0	63 (100)	NE (NE, NE)	NE (NE, NE) 0.9963	0.2759	
North America	58	5 (8.6)	53 (91.4)	NE (NE, NE)	28	5 (17.9)	23 (82.1)	NE (3.9, NE)	0.3870 (0.1115, 1.3436) 0.1350	0.1225	
Europe + Israel	166	5 (3.0)	161 (97.0)	NE (NE, NE)	81	0	81 (100)	NE (NE, NE)	NE (NE, NE) 0.9954	0.1637	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Vision blurred

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.2890
0	199	7 (3.5)	192 (96.5)	NE (NE, NE)	95	4 (4.2)	91 (95.8)	NE (NE, NE)	0.7057 (0.2054, 2.4239) 0.5798	0.5784	
1	172	6 (3.5)	166 (96.5)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	2.2666 (0.2679, 19.1802) 0.4526	0.4402	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Eye disorders; PT: Vision blurred

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.2323
0	60	3 (5.0)	57 (95.0)	NE (NE, NE)	31	1 (3.2)	30 (96.8)	NE (NE, NE)	0.9152 (0.0884, 9.4724) 0.9408	0.9407	
1	107	3 (2.8)	104 (97.2)	NE (NE, NE)	48	1 (2.1)	47 (97.9)	NE (NE, NE)	1.3371 (0.1390, 12.8592) 0.8014	0.8007	
2	114	3 (2.6)	111 (97.4)	NE (NE, NE)	50	3 (6.0)	47 (94.0)	NE (NE, NE)	0.3729 (0.0749, 1.8568) 0.2284	0.2102	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Vision blurred

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 4 (4.4)	86 (95.6)	NE (NE, NE)	43 0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9955	0.1683	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Vision blurred

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.2836
PD	173	5 (2.9)	168 (97.1)	NE (NE, NE)	77	4 (5.2)	73 (94.8)	NE (NE, NE)	0.5040 (0.1347, 1.8861)	0.2998	
PR	48	2 (4.2)	46 (95.8)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	0.3089 (NE, NE)	0.4119	
SD	82	3 (3.7)	79 (96.3)	NE (NE, NE)	54	1 (1.9)	53 (98.1)	NE (NE, NE)	1.4468 (0.1458, 14.3614)	0.7511	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Vision blurred

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.2970
Yes	37	2 (5.4)	35 (94.6)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9972	0.4249	
No	334	11 (3.3)	323 (96.7)	NE (NE, NE)	159	5 (3.1)	154 (96.9)	NE (NE, NE)	0.8908 (0.3065, 2.5885) 0.8317	0.8322	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Vision blurred

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.3564
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	1 (14.3)	6 (85.7)	NE (3.9, NE)	0.2620 (0.0163, 4.2050)	0.3442	0.3088
No	347	12 (3.5)	335 (96.5)	NE (NE, NE)	165	4 (2.4)	161 (97.6)	NE (NE, NE)	1.2315 (0.3941, 3.8479)	0.7191	0.7202

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Vision blurred

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.3980
Normal Function	201	7 (3.5)	194 (96.5)	NE (NE, NE)	80	3 (3.8)	77 (96.3)	NE (NE, NE)	0.8371 (0.2158, 3.2476) 0.7972	0.7969	
Mild Impairment	123	4 (3.3)	119 (96.7)	NE (NE, NE)	65	2 (3.1)	63 (96.9)	NE (NE, NE)	0.7744 (0.1336, 4.4903) 0.7756	0.7750	
Moderate Impairment	41	2 (4.9)	39 (95.1)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9968	0.3157	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Vision blurred

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.3423
Normal Function	170	4 (2.4)	166 (97.6)	NE (NE, NE)	88	3 (3.4)	85 (96.6)	NE (NE, NE)	0.6625 (0.1482, 2.9616) 0.5900	0.5887	
Mild Impairment	194	9 (4.6)	185 (95.4)	NE (NE, NE)	82	2 (2.4)	80 (97.6)	NE (NE, NE)	1.5114 (0.3227, 7.0791) 0.6001	0.5971	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Vision blurred

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1239
Yes	331	13 (3.9)	318 (96.1)	NE (NE, NE)	146	4 (2.7)	142 (97.3)	NE (NE, NE)	1.2469 (0.4041, 3.8470) 0.7011	0.7007	
No	40	0	40 (100)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	0.0000 (0.0000, ) 0.9975	0.2024	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Vision blurred

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											
Positive	329	11 (3.3)	318 (96.7)	NE (NE, NE)	152	4 (2.6)	148 (97.4)	NE (NE, NE)	1.1389 (0.3619, 3.5839) 0.8241	0.8242	0.8473
Negative	42	2 (4.8)	40 (95.2)	NE (12.4, NE)	20	1 (5.0)	19 (95.0)	NE (NE, NE)	0.4880 (0.0305, 7.8030) 0.6119	0.6043	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Vision blurred

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.2520
Positive	331	11 (3.3)	320 (96.7)	NE (NE, NE)	155	5 (3.2)	150 (96.8)	NE (NE, NE)	0.9278 (0.3217, 2.6756)	0.8900	
Negative	40	2 (5.0)	38 (95.0)	NE (12.4, NE)	17	0	17 (100)	NE (NE, NE)	0.8896 (NE, NE) 0.9978	0.5145	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Dry eye

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0481
HER2 IHC 1+	214	2 (0.9)	212 (99.1)	NE (NE, NE)	100	3 (3.0)	97 (97.0)	NE (NE, NE)	0.2115 (0.0348, 1.2841) 0.0914	0.0635	
HER2 IHC 2+/ISH Negative	157	8 (5.1)	149 (94.9)	NE (NE, NE)	72	1 (1.4)	71 (98.6)	NE (11.8, NE)	2.3031 (0.2794, 18.9829) 0.4382	0.4256	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Dry eye

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.0125
1	220	4 (1.8)	216 (98.2)	NE (NE, NE)	94	4 (4.3)	90 (95.7)	NE (11.8, NE)	0.1917 (0.0450, 0.8165) 0.0255	0.0141	
>=2	150	6 (4.0)	144 (96.0)	NE (NE, NE)	78	0	78 (100)	NE (NE, NE)	NE (NE, NE) 0.9947	0.1053	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Dry eye

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Prior CDK4/6											0.9997
Yes	233	7 (3.0)	226 (97.0)	NE (NE, NE)	112	4 (3.6)	108 (96.4)	NE (11.8, NE)	0.4126 (0.1120, 1.5192) 0.1831	0.1714	
No	98	0	98 (100)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.8.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Eye disorders; PT: Dry eye

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5745
<65	289	7 (2.4)	282 (97.6)	NE (NE, NE)	126	3 (2.4)	123 (97.6)	NE (11.8, NE)	0.5577 (0.1355, 2.2965) 0.4187	0.4130	
>=65	82	3 (3.7)	79 (96.3)	NE (NE, NE)	46	1 (2.2)	45 (97.8)	NE (NE, NE)	1.4025 (0.1448, 13.5819) 0.7703	0.7692	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Dry eye

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0774
<75	357	8 (2.2)	349 (97.8)	NE (NE, NE)	163	4 (2.5)	159 (97.5)	NE (11.8, NE)	0.5343 (0.1523, 1.8742) 0.3276	0.3206	
>=75	14	2 (14.3)	12 (85.7)	NE (5.5, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9979	0.2751	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Dry eye

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.0479
White	175	8 (4.6)	167 (95.4)	NE (NE, NE)	85	1 (1.2)	84 (98.8)	NE (NE, NE)	2.8154 (0.3449, 22.9803) 0.3339	0.3132	
Non-White	196	2 (1.0)	194 (99.0)	NE (NE, NE)	86	3 (3.5)	83 (96.5)	NE (11.8, NE)	0.1263 (0.0201, 0.7952) 0.0275	0.0102	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Dry eye

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.4932
Asia	147	2 (1.4)	145 (98.6)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (11.8, NE)	0.3014 (0.0260, 3.4879) 0.3371	0.3105	
North America	58	2 (3.4)	56 (96.6)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9973	0.4270	
Europe + Israel	166	6 (3.6)	160 (96.4)	NE (NE, NE)	81	3 (3.7)	78 (96.3)	NE (NE, NE)	0.7159 (0.1747, 2.9338) 0.6424	0.6410	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Dry eye

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.1276
0	199	7 (3.5)	192 (96.5)	NE (NE, NE)	95	4 (4.2)	91 (95.8)	NE (11.8, NE)	0.5438 (0.1545, 1.9147) 0.3429	0.3361	
1	172	3 (1.7)	169 (98.3)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE) 0.9957	0.4468	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Dry eye

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)									0.0351
0	60	2 (3.3)	58 (96.7) NE (NE, NE)	31	0	31 (100) NE (NE, NE)	NE (NE, NE) 0.9971	0.3983	
1	107	0	107 (100) NE (NE, NE)	48	2 (4.2)	46 (95.8) NE (NE, NE)	0.0000 (0.0000, ) 0.9972	0.0177	
2	114	4 (3.5)	110 (96.5) NE (NE, NE)	50	0	50 (100) NE (NE, NE)	NE (NE, NE) 0.9959	0.2215	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Dry eye

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 (4.4)	86 (95.6)	NE (NE, NE)	43 (4.7)	41 (95.3)	11.8 (11.8, NE)	0.3254 (0.0519, 2.0407) 0.2307	0.2138	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Dry eye

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.4869
PD	173	5 (2.9)	168 (97.1)	NE (NE, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	0.6048 (0.1108, 3.3032)	0.5578	
PR	48	2 (4.2)	46 (95.8)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	0.5616 (NE, NE)	0.4151	
SD	82	2 (2.4)	80 (97.6)	NE (NE, NE)	54	2 (3.7)	52 (96.3)	NE (11.8, NE)	0.9972 (0.0478, 2.8440)	0.3224	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Eye disorders; PT: Dry eye

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.2965
Yes	37	2 (5.4)	35 (94.6)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9977	0.5228	
No	334	8 (2.4)	326 (97.6)	NE (NE, NE)	159	4 (2.5)	155 (97.5)	NE (NE, NE)	0.5761 (0.1668, 1.9903) 0.3833	0.3779	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Dry eye

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.2874
Yes	24	2 (8.3)	22 (91.7)	NE (11.1, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.6143	
No	347	8 (2.3)	339 (97.7)	NE (NE, NE)	165	4 (2.4)	161 (97.6)	NE (NE, NE)	0.6371 (0.1860, 2.1816) 0.4728	0.4696	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Dry eye

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0445
Normal Function	201	5 (2.5)	196 (97.5)	NE (NE, NE)	80	3 (3.8)	77 (96.3)	NE (11.8, NE)	0.2816 (0.0595, 1.3339) 0.1103	0.0927	
Mild Impairment	123	5 (4.1)	118 (95.9)	NE (NE, NE)	65	0	65 (100)	NE (NE, NE)	NE 0.9953	0.1540	
Moderate Impairment	41	0	41 (100)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	0.0000 (0.0000, ) 0.9977	0.1510	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Dry eye

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Hepatic function at baseline											
Normal Function	170	5 (2.9)	165 (97.1)	NE (NE, NE)	88	2 (2.3)	86 (97.7)	NE (11.8, NE)	0.8019 (0.1482, 4.3391) 0.7978	0.7974	0.8481
Mild Impairment	194	5 (2.6)	189 (97.4)	NE (NE, NE)	82	2 (2.4)	80 (97.6)	NE (NE, NE)	0.6068 (0.1111, 3.3137) 0.5641	0.5605	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Dry eye

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.9999
Yes	331	10 (3.0)	321 (97.0)	NE (NE, NE)	146	4 (2.7)	142 (97.3)	NE (NE, NE)	0.6984 (0.2129, 2.2909)	0.5537	
No	40	0	40 (100)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE)	NE	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Dry eye

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.1182
Positive	329	7 (2.1)	322 (97.9)	NE (NE, NE)	152	4 (2.6)	148 (97.4)	NE (NE, NE)	0.4506 (0.1259, 1.6126) 0.2204	0.2099	
Negative	42	3 (7.1)	39 (92.9)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) 0.9963	0.2746	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Eye disorders; PT: Dry eye

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.1460
Positive	331	7 (2.1)	324 (97.9)	NE (NE, NE)	155	4 (2.6)	151 (97.4)	NE (NE, NE)	0.4559 (0.1273, 1.6330)	0.2173	
Negative	40	3 (7.5)	37 (92.5)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	0.2276 (NE, NE) 0.9966	0.3251	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0371
HER2 IHC 1+	214	28 (13.1)	186 (86.9)	NE (NE, NE)	100	5 (5.0)	95 (95.0)	NE (NE, NE)	2.0683 (0.7922, 5.4002) 0.1378	0.1293	
HER2 IHC 2+/ISH Negative	157	19 (12.1)	138 (87.9)	NE (NE, NE)	72	11 (15.3)	61 (84.7)	NE (NE, NE)	0.6022 (0.2833, 1.2798) 0.1873	0.1844	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.6545
1	220	31 (14.1)	189 (85.9)	NE (NE, NE)	94	9 (9.6)	85 (90.4)	NE (NE, NE)	1.1985 (0.5670, 2.5333) 0.6354	0.6292	
>=2	150	16 (10.7)	134 (89.3)	NE (NE, NE)	78	7 (9.0)	71 (91.0)	NE (8.3, NE)	0.8430 (0.3399, 2.0907) 0.7125	0.7122	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.6985
Yes	233	32 (13.7)	201 (86.3)	NE (NE, NE)	112	10 (8.9)	102 (91.1)	NE (NE, NE)	1.1635 (0.5655, 2.3940) 0.6808	0.6759	
No	98	10 (10.2)	88 (89.8)	NE (NE, NE)	43	4 (9.3)	39 (90.7)	NE (NE, NE)	0.8593 (0.2668, 2.7676) 0.7995	0.7993	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8313
<65	289	37 (12.8)	252 (87.2)	NE (NE, NE)	126	12 (9.5)	114 (90.5)	NE (NE, NE)	1.0143 (0.5236, 1.9649) 0.9664	0.9647	
>=65	82	10 (12.2)	72 (87.8)	NE (NE, NE)	46	4 (8.7)	42 (91.3)	NE (NE, NE)	1.2110 (0.3768, 3.8919) 0.7479	0.7469	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1637
<75	357	45 (12.6)	312 (87.4)	NE (NE, NE)	163	16 (9.8)	147 (90.2)	NE (NE, NE)	0.9746 (0.5461, 1.7392) 0.9306	0.9334	
>=75	14	2 (14.3)	12 (85.7)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9978	0.2525	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.8001
White	175	27 (15.4)	148 (84.6)	NE (NE, NE)	85	9 (10.6)	76 (89.4)	NE (NE, NE)	1.1063 (0.5157, 2.3735) 0.7953	0.7914	
Non-White	196	20 (10.2)	176 (89.8)	NE (NE, NE)	86	7 (8.1)	79 (91.9)	NE (NE, NE)	1.0130 (0.4240, 2.4205) 0.9767	0.9780	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.3952
Asia	147	14 (9.5)	133 (90.5)	NE (NE, NE)	63	6 (9.5)	57 (90.5)	NE (8.3, NE)	0.7579 (0.2867, 2.0033) 0.5762	0.5739	
North America	58	11 (19.0)	47 (81.0)	NE (NE, NE)	28	5 (17.9)	23 (82.1)	NE (NE, NE)	0.7707 (0.2619, 2.2679) 0.6362	0.6392	
Europe + Israel	166	22 (13.3)	144 (86.7)	NE (NE, NE)	81	5 (6.2)	76 (93.8)	NE (NE, NE)	1.7236 (0.6470, 4.5919) 0.2762	0.2700	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.5460
0	199	17 (8.5)	182 (91.5)	NE (NE, NE)	95	7 (7.4)	88 (92.6)	NE (NE, NE)	0.9252 (0.3807, 2.2487) 0.8638	0.8667	
1	172	30 (17.4)	142 (82.6)	NE (NE, NE)	77	9 (11.7)	68 (88.3)	NE (8.3, NE)	1.1453 (0.5371, 2.4419) 0.7255	0.7270	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.3457
0	60	9 (15.0)	51 (85.0)	NE (NE, NE)	31	3 (9.7)	28 (90.3)	NE (NE, NE)	1.3406 (0.3603, 4.9879) 0.6619	0.6621	
1	107	17 (15.9)	90 (84.1)	NE (NE, NE)	48	3 (6.3)	45 (93.8)	NE (NE, NE)	2.4255 (0.7097, 8.2892) 0.1576	0.1440	
2	114	13 (11.4)	101 (88.6)	NE (NE, NE)	50	6 (12.0)	44 (88.0)	NE (NE, NE)	0.5779 (0.2121, 1.5749) 0.2837	0.2788	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	8 (8.9)	82 (91.1) NE (NE, NE)	43	4 (9.3)	39 (90.7) NE (8.3, NE)	0.6051 (0.1731, 2.1155) 0.4315	0.4289	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.3367
PD	173	16 (9.2)	157 (90.8)	NE (NE, NE)	77	8 (10.4)	69 (89.6)	NE (NE, NE)	0.7056 (0.2976, 1.6732)	0.4269	
PR	48	5 (10.4)	43 (89.6)	NE (NE, NE)	21	2 (9.5)	19 (90.5)	NE (NE, NE)	0.4286 (0.1382, 3.9314)	0.7201	
SD	82	16 (19.5)	66 (80.5)	NE (NE, NE)	54	5 (9.3)	49 (90.7)	NE (8.3, NE)	0.7370 (0.7209, 1.7753)	0.2605	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.8161
Yes	37	3 (8.1)	34 (91.9)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	1.0250 (0.1066, 9.8588)	0.9829	
No	334	44 (13.2)	290 (86.8)	NE (NE, NE)	159	15 (9.4)	144 (90.6)	NE (NE, NE)	1.0663 (0.5888, 1.9310)	0.8295	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.5011
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9981	0.5892	
No	347	46 (13.3)	301 (86.7)	NE (NE, NE)	165	16 (9.7)	149 (90.3)	NE (NE, NE)	1.0448 (0.5870, 1.8596) 0.8816	0.8778	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.2990
Normal Function	201	26 (12.9)	175 (87.1)	NE (NE, NE)	80	11 (13.8)	69 (86.3)	NE (8.3, NE)	0.7025 (0.3422, 1.4421) 0.3359	0.3356	
Mild Impairment	123	14 (11.4)	109 (88.6)	NE (NE, NE)	65	3 (4.6)	62 (95.4)	NE (NE, NE)	1.9762 (0.5613, 6.9581) 0.2889	0.2790	
Moderate Impairment	41	6 (14.6)	35 (85.4)	NE (NE, NE)	23	2 (8.7)	21 (91.3)	NE (NE, NE)	1.5372 (0.3101, 7.6215) 0.5986	0.5956	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.7702
Normal Function	170	25 (14.7)	145 (85.3)	NE (NE, NE)	88	9 (10.2)	79 (89.8)	NE (NE, NE)	1.0853 (0.5009, 2.3518) 0.8356	0.8368	
Mild Impairment	194	21 (10.8)	173 (89.2)	NE (NE, NE)	82	7 (8.5)	75 (91.5)	NE (NE, NE)	1.0028 (0.4224, 2.3805) 0.9950	0.9912	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.8016
Yes	331	41 (12.4)	290 (87.6)	NE (NE, NE)	146	14 (9.6)	132 (90.4)	NE (NE, NE)	1.0279 (0.5567, 1.8979) 0.9299	0.9262	
No	40	6 (15.0)	34 (85.0)	NE (NE, NE)	26	2 (7.7)	24 (92.3)	NE (NE, NE)	1.2679 (0.2447, 6.5685) 0.7773	0.7768	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.8971
Positive	329	42 (12.8)	287 (87.2)	NE (NE, NE)	152	14 (9.2)	138 (90.8)	NE (NE, NE)	1.0664 (0.5782, 1.9669) 0.8369	0.8333	
Negative	42	5 (11.9)	37 (88.1)	NE (NE, NE)	20	2 (10.0)	18 (90.0)	NE (NE, NE)	0.9824 (0.1866, 5.1724) 0.9832	0.9797	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.7544
Positive	331	42 (12.7)	289 (87.3)	NE (NE, NE)	155	14 (9.0)	141 (91.0)	NE (NE, NE)	1.0834 (0.5873, 1.9984) 0.7977	0.7941	
Negative	40	5 (12.5)	35 (87.5)	NE (NE, NE)	17	2 (11.8)	15 (88.2)	NE (NE, NE)	0.8408 (0.1583, 4.4657) 0.8387	0.8342	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Insomnia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.3254
HER2 IHC 1+	214	15 (7.0)	199 (93.0)	NE (NE, NE)	100	4 (4.0)	96 (96.0)	NE (NE, NE)	1.3050 (0.4271, 3.9868) 0.6404	0.6391	
HER2 IHC 2+/ISH Negative	157	9 (5.7)	148 (94.3)	NE (NE, NE)	72	5 (6.9)	67 (93.1)	NE (NE, NE)	0.6872 (0.2282, 2.0697) 0.5049	0.5041	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Insomnia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.8639
1	220	15 (6.8)	205 (93.2)	NE (NE, NE)	94	5 (5.3)	89 (94.7)	NE (NE, NE)	1.0000 (0.3597, 2.7802)	0.9965	
>=2	150	9 (6.0)	141 (94.0)	NE (NE, NE)	78	4 (5.1)	74 (94.9)	NE (NE, NE)	0.9333 (0.2818, 3.0905)	0.9092	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Insomnia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.7596
Yes	233	13 (5.6)	220 (94.4)	NE (NE, NE)	112	5 (4.5)	107 (95.5)	NE (NE, NE)	0.9552 (0.3361, 2.7151) 0.9315	0.9349	
No	98	7 (7.1)	91 (92.9)	NE (NE, NE)	43	2 (4.7)	41 (95.3)	NE (NE, NE)	1.1961 (0.2455, 5.8275) 0.8246	0.8244	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Insomnia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7404
<65	289	21 (7.3)	268 (92.7)	NE (NE, NE)	126	7 (5.6)	119 (94.4)	NE (NE, NE)	1.0123 (0.4256, 2.4081) 0.9779	0.9770	
>=65	82	3 (3.7)	79 (96.3)	NE (NE, NE)	46	2 (4.3)	44 (95.7)	NE (NE, NE)	0.7094 (0.1172, 4.2948) 0.7086	0.7073	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Insomnia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3121
<75	357	23 (6.4)	334 (93.6)	NE (NE, NE)	163	9 (5.5)	154 (94.5)	NE (NE, NE)	0.9016 (0.4128, 1.9690) 0.7948	0.7962	
>=75	14	1 (7.1)	13 (92.9)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9985	0.4142	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Insomnia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.2267
White	175	10 (5.7)	165 (94.3)	NE (NE, NE)	85	6 (7.1)	79 (92.9)	NE (NE, NE)	0.5888 (0.2104, 1.6480) 0.3131	0.3088	
Non-White	196	14 (7.1)	182 (92.9)	NE (NE, NE)	86	3 (3.5)	83 (96.5)	NE (NE, NE)	1.7356 (0.4954, 6.0807) 0.3887	0.3825	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Insomnia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.3913
Asia	147	11 (7.5)	136 (92.5)	NE (NE, NE)	63	3 (4.8)	60 (95.2)	NE (NE, NE)	1.2721 (0.3511, 4.6093) 0.7141	0.7134	
North America	58	6 (10.3)	52 (89.7)	NE (NE, NE)	28	1 (3.6)	27 (96.4)	NE (NE, NE)	2.3803 (0.2842, 19.9332) 0.4238	0.4095	
Europe + Israel	166	7 (4.2)	159 (95.8)	NE (NE, NE)	81	5 (6.2)	76 (93.8)	NE (NE, NE)	0.5003 (0.1556, 1.6084) 0.2451	0.2364	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Insomnia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.7743
0	199	12 (6.0)	187 (94.0)	NE (NE, NE)	95	4 (4.2)	91 (95.8)	NE (NE, NE)	1.0996 (0.3510, 3.4447) 0.8706	0.8700	
1	172	12 (7.0)	160 (93.0)	NE (NE, NE)	77	5 (6.5)	72 (93.5)	NE (NE, NE)	0.8432 (0.2918, 2.4361) 0.7526	0.7514	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.8.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Psychiatric disorders; PT: Insomnia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.3617
0	60	5 (8.3)	55 (91.7)	NE (NE, NE)	31	2 (6.5)	29 (93.5)	NE (NE, NE)	1.1633 (0.2235, 6.0547) 0.8574	0.8594	
1	107	11 (10.3)	96 (89.7)	NE (NE, NE)	48	2 (4.2)	46 (95.8)	NE (NE, NE)	2.1910 (0.4844, 9.9105) 0.3084	0.2956	
2	114	5 (4.4)	109 (95.6)	NE (NE, NE)	50	2 (4.0)	48 (96.0)	NE (NE, NE)	0.5911 (0.1072, 3.2582) 0.5460	0.5418	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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SOC: Psychiatric disorders; PT: Insomnia

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 (3.3)	87 (96.7)	NE (NE, NE)	43 (7.0)	40 (93.0)	NE (NE, NE)	0.4081 (0.0818, 2.0368) 0.2745	0.2605	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Insomnia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.5188
PD	173	10 (5.8)	163 (94.2)	NE (NE, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	1.2068 (0.3276, 4.4464) 0.7775	0.7768	
PR	48	2 (4.2)	46 (95.8)	NE (NE, NE)	21	2 (9.5)	19 (90.5)	NE (NE, NE)	0.2805 (0.0377, 2.0844) 0.2141	0.1868	
SD	82	6 (7.3)	76 (92.7)	NE (NE, NE)	54	3 (5.6)	51 (94.4)	NE (NE, NE)	1.1679 (0.2881, 4.7349) 0.8279	0.8281	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Insomnia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.4849
Yes	37	1 (2.7)	36 (97.3)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.5637	
No	334	23 (6.9)	311 (93.1)	NE (NE, NE)	159	9 (5.7)	150 (94.3)	NE (NE, NE)	0.9445 (0.4329, 2.0605) 0.8859	0.8874	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Insomnia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.4753
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9981	0.5892	
No	347	23 (6.6)	324 (93.4)	NE (NE, NE)	165	9 (5.5)	156 (94.5)	NE (NE, NE)	0.9306 (0.4263, 2.0316) 0.8567	0.8583	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Psychiatric disorders; PT: Insomnia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.9049
Normal Function	201	16 (8.0)	185 (92.0)	NE (NE, NE)	80	6 (7.5)	74 (92.5)	NE (NE, NE)	0.8608 (0.3335, 2.2214) 0.7566	0.7578	
Mild Impairment	123	6 (4.9)	117 (95.1)	NE (NE, NE)	65	2 (3.1)	63 (96.9)	NE (NE, NE)	1.0916 (0.2126, 5.6040) 0.9164	0.9157	
Moderate Impairment	41	2 (4.9)	39 (95.1)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	0.9414 (0.0851, 10.4093) 0.9607	0.9607	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Insomnia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.5718
Normal Function	170	14 (8.2)	156 (91.8)	NE (NE, NE)	88	5 (5.7)	83 (94.3)	NE (NE, NE)	1.1031 (0.3916, 3.1072) 0.8526	0.8520	
Mild Impairment	194	9 (4.6)	185 (95.4)	NE (NE, NE)	82	4 (4.9)	78 (95.1)	NE (NE, NE)	0.7582 (0.2311, 2.4879) 0.6480	0.6487	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Insomnia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.7637
Yes	331	21 (6.3)	310 (93.7)	NE (NE, NE)	146	8 (5.5)	138 (94.5)	NE (NE, NE)	0.9297 (0.4087, 2.1152) 0.8621	0.8639	
No	40	3 (7.5)	37 (92.5)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	1.1831 (0.1107, 12.6390) 0.8894	0.8893	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Insomnia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.7704
Positive	329	20 (6.1)	309 (93.9)	NE (NE, NE)	152	7 (4.6)	145 (95.4)	NE (NE, NE)	1.0025 (0.4197, 2.3942) 0.9956	0.9938	
Negative	42	4 (9.5)	38 (90.5)	NE (NE, NE)	20	2 (10.0)	18 (90.0)	NE (NE, NE)	0.8371 (0.1500, 4.6718) 0.8394	0.8348	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Psychiatric disorders; PT: Insomnia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.6427
Positive	331	20 (6.0)	311 (94.0)	NE (NE, NE)	155	7 (4.5)	148 (95.5)	NE (NE, NE)	1.0191 (0.4267, 2.4342)	0.9660	0.9640
Negative	40	4 (10.0)	36 (90.0)	NE (NE, NE)	17	2 (11.8)	15 (88.2)	NE (NE, NE)	0.7319 (0.1304, 4.1083)	0.7229	0.7170

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Anxiety

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0183
HER2 IHC 1+	214	6 (2.8)	208 (97.2)	NE (NE, NE)	100	0	100 (100)	NE (NE, NE)	NE (NE, NE) 0.9948	0.1213	
HER2 IHC 2+/ISH Negative	157	6 (3.8)	151 (96.2)	NE (NE, NE)	72	5 (6.9)	67 (93.1)	NE (NE, NE)	0.3477 (0.1034, 1.1689) 0.0877	0.0750	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Anxiety

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.2005
1	220	9 (4.1)	211 (95.9)	NE (NE, NE)	94	2 (2.1)	92 (97.9)	NE (NE, NE)	1.4822 (0.3178, 6.9140) 0.6165	0.6139	
>=2	150	3 (2.0)	147 (98.0)	NE (NE, NE)	78	3 (3.8)	75 (96.2)	NE (8.3, NE)	0.3307 (0.0633, 1.7274) 0.1896	0.1701	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Psychiatric disorders; PT: Anxiety

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.7859
Yes	233	9 (3.9)	224 (96.1)	NE (NE, NE)	112	3 (2.7)	109 (97.3)	NE (NE, NE)	1.0391 (0.2761, 3.9107) 0.9547	0.9543	
No	98	2 (2.0)	96 (98.0)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	0.6386 (0.0567, 7.1972) 0.7167	0.7147	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Anxiety

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0339
<65	289	8 (2.8)	281 (97.2)	NE (NE, NE)	126	5 (4.0)	121 (96.0)	NE (NE, NE)	0.4347 (0.1384, 1.3657) 0.1538	0.1431	
>=65	82	4 (4.9)	78 (95.1)	NE (NE, NE)	46	0	46 (100)	NE (NE, NE)	NE (NE, NE) 0.9954	0.1470	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Anxiety

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9999
<75	357	12 (3.4)	345 (96.6)	NE (NE, NE)	163	5 (3.1)	158 (96.9)	NE (NE, NE)	0.7709 (0.2675, 2.2215) 0.6299	0.6291	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Anxiety

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.5031
White	175	9 (5.1)	166 (94.9)	NE (NE, NE)	85	3 (3.5)	82 (96.5)	NE (NE, NE)	1.0790 (0.2891, 4.0274) 0.9100	0.9099	
Non-White	196	3 (1.5)	193 (98.5)	NE (NE, NE)	86	2 (2.3)	84 (97.7)	NE (NE, NE)	0.4273 (0.0682, 2.6763) 0.3637	0.3507	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Anxiety

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.0395
Asia	147	0	147 (100)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (8.3, NE)	0.0000 (0.0000, ) 0.9978	0.0052	
North America	58	3 (5.2)	55 (94.8)	NE (NE, NE)	28	3 (10.7)	25 (89.3)	NE (NE, NE)	0.3573 (0.0717, 1.7796) 0.2090	0.1897	
Europe + Israel	166	9 (5.4)	157 (94.6)	NE (NE, NE)	81	1 (1.2)	80 (98.8)	NE (NE, NE)	3.2484 (0.4071, 25.9219) 0.2662	0.2396	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Anxiety

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.7622
0	199	4 (2.0)	195 (98.0)	NE (NE, NE)	95	2 (2.1)	93 (97.9)	NE (NE, NE)	0.7238 (0.1305, 4.0159) 0.7116	0.7105	
1	172	8 (4.7)	164 (95.3)	NE (NE, NE)	77	3 (3.9)	74 (96.1)	NE (8.3, NE)	0.8548 (0.2221, 3.2905) 0.8196	0.8194	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Anxiety

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.4196
0	60	4 (6.7)	56 (93.3)	NE (NE, NE)	31	1 (3.2)	30 (96.8)	NE (NE, NE)	1.6238 (0.1801, 14.6380) 0.6657	0.6627	
1	107	2 (1.9)	105 (98.1)	NE (NE, NE)	48	0	48 (100)	NE (NE, NE)	NE (NE, NE) 0.9970	0.3633	
2	114	4 (3.5)	110 (96.5)	NE (NE, NE)	50	3 (6.0)	47 (94.0)	NE (NE, NE)	0.3706 (0.0789, 1.7417) 0.2087	0.1923	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Anxiety

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 (2.2)	88 (97.8)	NE (NE, NE)	43 (2.3)	42 (97.7)	NE (8.3, NE)	0.4226 (0.0354, 5.0445) 0.4960	0.4843	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Anxiety

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.0192
PD	173	2 (1.2)	171 (98.8)	NE (NE, NE)	77	4 (5.2)	73 (94.8)	NE (NE, NE)	0.1711 (0.0311, 0.9413)	0.0217	
PR	48	2 (4.2)	46 (95.8)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	0.0424 (NE, NE)	0.3627	
SD	82	7 (8.5)	75 (91.5)	NE (NE, NE)	54	1 (1.9)	53 (98.1)	NE (8.3, NE)	3.1707 (0.3838, 26.1925)	0.2588	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Anxiety

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.2862
Yes	37	2 (5.4)	35 (94.6)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9972	0.4186	
No	334	10 (3.0)	324 (97.0)	NE (NE, NE)	159	5 (3.1)	154 (96.9)	NE (NE, NE)	0.6553 (0.2204, 1.9489) 0.4472	0.4443	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Psychiatric disorders; PT: Anxiety

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.9999
Yes	24	0	24 (100)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE)	NE	
No	347	12 (3.5)	335 (96.5)	NE (NE, NE)	165	5 (3.0)	160 (97.0)	NE (NE, NE)	0.8106 (0.2815, 2.3336)	0.6966	0.6971

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Anxiety

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0243
Normal Function	201	5 (2.5)	196 (97.5)	NE (NE, NE)	80	5 (6.3)	75 (93.8)	NE (NE, NE)	0.2425 (0.0670, 0.8774) 0.0308	0.0203	
Mild Impairment	123	5 (4.1)	118 (95.9)	NE (NE, NE)	65	0	65 (100)	NE (NE, NE)	NE (NE, NE) 0.9951	0.1294	
Moderate Impairment	41	1 (2.4)	40 (97.6)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9979	0.5308	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Anxiety

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.5131
Normal Function	170	7 (4.1)	163 (95.9)	NE (NE, NE)	88	4 (4.5)	84 (95.5)	NE (NE, NE)	0.6744 (0.1944, 2.3403) 0.5349	0.5326	
Mild Impairment	194	5 (2.6)	189 (97.4)	NE (NE, NE)	82	1 (1.2)	81 (98.8)	NE (NE, NE)	1.4739 (0.1677, 12.9571) 0.7265	0.7247	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Psychiatric disorders; PT: Anxiety

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1910
Yes	331	10 (3.0)	321 (97.0)	NE (NE, NE)	146	5 (3.4)	141 (96.6)	NE (NE, NE)	0.6588 (0.2221, 1.9540) 0.4519	0.4490	
No	40	2 (5.0)	38 (95.0)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9972	0.4209	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Psychiatric disorders; PT: Anxiety

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.5221
Positive	329	11 (3.3)	318 (96.7)	NE (NE, NE)	152	4 (2.6)	148 (97.4)	NE (NE, NE)	0.9251 (0.2906, 2.9449) 0.8952	0.8952	
Negative	42	1 (2.4)	41 (97.6)	NE (NE, NE)	20	1 (5.0)	19 (95.0)	NE (NE, NE)	0.3100 (0.0189, 5.0962) 0.4122	0.3869	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Psychiatric disorders; PT: Anxiety

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.4413
Positive	331	11 (3.3)	320 (96.7)	NE (NE, NE)	155	4 (2.6)	151 (97.4)	NE (NE, NE)	0.9408 (0.2955, 2.9956)	0.9178	
Negative	40	1 (2.5)	39 (97.5)	NE (NE, NE)	17	1 (5.9)	16 (94.1)	NE (2.5, NE)	0.2282 (0.0138, 3.7759)	0.2614	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.9285
HER2 IHC 1+	214	27 (12.6)	187 (87.4)	NE (NE, NE)	100	17 (17.0)	83 (83.0)	NE (NE, NE)	0.4008 (0.2127, 0.7551) 0.0047	0.0040	
HER2 IHC 2+/ISH Negative	157	17 (10.8)	140 (89.2)	NE (23.9, NE)	72	12 (16.7)	60 (83.3)	NE (NE, NE)	0.3711 (0.1725, 0.7985) 0.0112	0.0088	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.4188
1	220	20 (9.1)	200 (90.9)	NE (NE, NE)	94	15 (16.0)	79 (84.0)	NE (NE, NE)	0.3613 (0.1809, 0.7217) 0.0039	0.0030	
>=2	150	24 (16.0)	126 (84.0)	23.9 (17.4, NE)	78	14 (17.9)	64 (82.1)	NE (NE, NE)	0.4118 (0.2052, 0.8264) 0.0125	0.0108	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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DE.T.4.8.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.2312
Yes	233	23 (9.9)	210 (90.1)	NE (NE, NE)	112	12 (10.7)	100 (89.3)	NE (NE, NE)	0.5260 (0.2550, 1.0848) 0.0819	0.0785	
No	98	17 (17.3)	81 (82.7)	NE (19.7, NE)	43	14 (32.6)	29 (67.4)	NE (5.5, NE)	0.3101 (0.1498, 0.6416) 0.0016	0.0012	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3044
<65	289	28 (9.7)	261 (90.3)	NE (NE, NE)	126	19 (15.1)	107 (84.9)	NE (NE, NE)	0.3785 (0.2074, 0.6907) 0.0015	0.0012	
>=65	82	16 (19.5)	66 (80.5)	19.7 (16.2, 23.9)	46	10 (21.7)	36 (78.3)	NE (NE, NE)	0.4562 (0.1959, 1.0623) 0.0688	0.0634	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7183
<75	357	42 (11.8)	315 (88.2)	NE (23.9, NE)	163	27 (16.6)	136 (83.4)	NE (NE, NE)	0.3774 (0.2275, 0.6262) 0.0002	0.0001	
>=75	14	2 (14.3)	12 (85.7)	NE (5.1, NE)	9	2 (22.2)	7 (77.8)	NE (0.0, NE)	0.5373 (0.0753, 3.8331) 0.5355	0.5290	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.0019
White	175	20 (11.4)	155 (88.6)	NE (NE, NE)	85	5 (5.9)	80 (94.1)	NE (NE, NE)	1.0677 (0.3929, 2.9011) 0.8978	0.8983	
Non-White	196	24 (12.2)	172 (87.8)	NE (19.7, NE)	86	24 (27.9)	62 (72.1)	NE (NE, NE)	0.2323 (0.1279, 0.4217) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.0050
Asia	147	18 (12.2)	129 (87.8)	23.9 (19.7, NE)	63	20 (31.7)	43 (68.3)	NE (NE, NE)	0.1870 (0.0949, 0.3685) <0.0001	<0.0001	
North America	58	12 (20.7)	46 (79.3)	NE (11.2, NE)	28	4 (14.3)	24 (85.7)	NE (NE, NE)	0.7116 (0.2163, 2.3414) 0.5756	0.5740	
Europe + Israel	166	14 (8.4)	152 (91.6)	NE (NE, NE)	81	5 (6.2)	76 (93.8)	NE (NE, NE)	0.7966 (0.2802, 2.2644) 0.6697	0.6691	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.4427
0	199	27 (13.6)	172 (86.4)	NE (23.9, NE)	95	15 (15.8)	80 (84.2)	NE (NE, NE)	0.4693 (0.2439, 0.9033) 0.0235	0.0227	
1	172	17 (9.9)	155 (90.1)	NE (NE, NE)	77	14 (18.2)	63 (81.8)	NE (NE, NE)	0.2871 (0.1349, 0.6112) 0.0012	0.0007	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.2044
0	60	6 (10.0)	54 (90.0)	NE (17.4, NE)	31	9 (29.0)	22 (71.0)	NE (2.9, NE)	0.1809 (0.0615, 0.5325) 0.0019	0.0007	
1	107	10 (9.3)	97 (90.7)	NE (NE, NE)	48	9 (18.8)	39 (81.3)	NE (NE, NE)	0.3498 (0.1406, 0.8702) 0.0239	0.0216	
2	114	15 (13.2)	99 (86.8)	NE (NE, NE)	50	6 (12.0)	44 (88.0)	NE (NE, NE)	0.6636 (0.2490, 1.7683) 0.4122	0.4097	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	13 (14.4)	77 (85.6)	23.9 (19.7, NE)	43	5 (11.6)	38 (88.4)	NE (NE, NE)	0.4991 (0.1660, 1.5002) 0.2159	0.2090	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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 [c] Two-sided p-value from unstratified log-rank test.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.2086
PD	173	20 (11.6)	153 (88.4)	NE (23.9, NE)	77	10 (13.0)	67 (87.0)	NE (NE, NE)	0.4696 (0.2122, 1.0388)	0.0575	
PR	48	7 (14.6)	41 (85.4)	NE (16.5, NE)	21	7 (33.3)	14 (66.7)	NE (1.5, NE)	0.1583 (0.0475, 0.5274)	0.0008	
SD	82	9 (11.0)	73 (89.0)	NE (19.7, NE)	54	5 (9.3)	49 (90.7)	NE (NE, NE)	0.6500 (0.2065, 2.0459)	0.4676	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
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 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.6993
Yes	37	3 (8.1)	34 (91.9)	NE (17.4, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	0.5276 (0.0460, 6.0569)	0.6018	
No	334	41 (12.3)	293 (87.7)	NE (23.9, NE)	159	28 (17.6)	131 (82.4)	NE (NE, NE)	0.3823 (0.2317, 0.6307)	0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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DE.T.4.8.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.4676
Yes	24	4 (16.7)	20 (83.3)	17.4 (17.4, NE)	7	1 (14.3)	6 (85.7)	NE (0.4, NE)	0.6257 (0.0644, 6.0806) 0.6861	0.6835	
No	347	40 (11.5)	307 (88.5)	NE (23.9, NE)	165	28 (17.0)	137 (83.0)	NE (NE, NE)	0.3731 (0.2253, 0.6179) 0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0417
Normal Function	201	19 (9.5)	182 (90.5)	NE (NE, NE)	80	15 (18.8)	65 (81.3)	NE (NE, NE)	0.2526 (0.1229, 0.5195) 0.0002	<0.0001	
Mild Impairment	123	14 (11.4)	109 (88.6)	23.9 (23.9, NE)	65	9 (13.8)	56 (86.2)	NE (NE, NE)	0.4572 (0.1910, 1.0942) 0.0788	0.0757	
Moderate Impairment	41	11 (26.8)	30 (73.2)	16.2 (9.2, NE)	23	4 (17.4)	19 (82.6)	NE (NE, NE)	1.2888 (0.4096, 4.0545) 0.6644	0.6636	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.6325
Normal Function	170	29 (17.1)	141 (82.9)	23.9 (19.7, NE)	88	19 (21.6)	69 (78.4)	NE (NE, NE)	0.4521 (0.2479, 0.8246) 0.0096	0.0089	
Mild Impairment	194	15 (7.7)	179 (92.3)	NE (NE, NE)	82	10 (12.2)	72 (87.8)	NE (NE, NE)	0.3286 (0.1417, 0.7620) 0.0095	0.0071	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1366
Yes	331	36 (10.9)	295 (89.1)	NE (NE, NE)	146	20 (13.7)	126 (86.3)	NE (NE, NE)	0.4578 (0.2603, 0.8051) 0.0067	0.0059	
No	40	8 (20.0)	32 (80.0)	23.9 (23.9, NE)	26	9 (34.6)	17 (65.4)	NE (2.6, NE)	0.2263 (0.0794, 0.6454) 0.0055	0.0032	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.8062
Positive	329	40 (12.2)	289 (87.8)	NE (NE, NE)	152	26 (17.1)	126 (82.9)	NE (NE, NE)	0.4083 (0.2453, 0.6797)	0.0004	
Negative	42	4 (9.5)	38 (90.5)	23.9 (17.4, 23.9)	20	3 (15.0)	17 (85.0)	NE (3.0, NE)	0.2203 (0.0358, 1.3548)	0.0749	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.6291
Positive	331	40 (12.1)	291 (87.9)	NE (NE, NE)	155	26 (16.8)	129 (83.2)	NE (NE, NE)	0.4149 (0.2492, 0.6910)	0.0006	
Negative	40	4 (10.0)	36 (90.0)	23.9 (17.4, 23.9)	17	3 (17.6)	14 (82.4)	NE (3.0, NE)	0.1653 (0.0261, 1.0469)	0.0319	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.1251
HER2 IHC 1+	214	21 (9.8)	193 (90.2)	NE (NE, NE)	100	13 (13.0)	87 (87.0)	NE (NE, NE)	0.5583 (0.2761, 1.1288) 0.1046	0.1000	
HER2 IHC 2+/ISH Negative	157	22 (14.0)	135 (86.0)	NE (NE, NE)	72	6 (8.3)	66 (91.7)	NE (NE, NE)	1.1091 (0.4444, 2.7680) 0.8244	0.8234	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.0324
1	220	16 (7.3)	204 (92.7)	NE (NE, NE)	94	12 (12.8)	82 (87.2)	NE (NE, NE)	0.4010 (0.1876, 0.8571) 0.0184	0.0148	
>=2	150	26 (17.3)	124 (82.7)	NE (NE, NE)	78	7 (9.0)	71 (91.0)	NE (NE, NE)	1.3842 (0.5936, 3.2279) 0.4517	0.4485	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.8149
Yes	233	29 (12.4)	204 (87.6)	NE (NE, NE)	112	13 (11.6)	99 (88.4)	NE (NE, NE)	0.7243 (0.3715, 1.4123) 0.3438	0.3414	
No	98	8 (8.2)	90 (91.8)	NE (NE, NE)	43	4 (9.3)	39 (90.7)	NE (NE, NE)	0.6394 (0.1893, 2.1592) 0.4713	0.4685	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4161
<65	289	33 (11.4)	256 (88.6)	NE (NE, NE)	126	15 (11.9)	111 (88.1)	NE (NE, NE)	0.6406 (0.3433, 1.1954) 0.1617	0.1593	
>=65	82	10 (12.2)	72 (87.8)	NE (NE, NE)	46	4 (8.7)	42 (91.3)	NE (NE, NE)	1.1455 (0.3572, 3.6738) 0.8193	0.8191	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8576
<75	357	42 (11.8)	315 (88.2)	NE (NE, NE)	163	18 (11.0)	145 (89.0)	NE (NE, NE)	0.7339 (0.4182, 1.2880) 0.2811	0.2798	
>=75	14	1 (7.1)	13 (92.9)	NE (8.4, NE)	9	1 (11.1)	8 (88.9)	NE (0.7, NE)	0.4804 (0.0287, 8.0452) 0.6101	0.6028	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.4549
White	175	26 (14.9)	149 (85.1)	NE (NE, NE)	85	10 (11.8)	75 (88.2)	NE (NE, NE)	0.8682 (0.4137, 1.8221) 0.7086	0.7097	
Non-White	196	17 (8.7)	179 (91.3)	NE (NE, NE)	86	9 (10.5)	77 (89.5)	NE (NE, NE)	0.5837 (0.2564, 1.3291) 0.1997	0.1942	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.7337
Asia	147	7 (4.8)	140 (95.2)	NE (NE, NE)	63	4 (6.3)	59 (93.7)	NE (NE, NE)	0.4214 (0.1176, 1.5098) 0.1844	0.1727	
North America	58	13 (22.4)	45 (77.6)	NE (11.8, NE)	28	6 (21.4)	22 (78.6)	NE (3.7, NE)	0.7511 (0.2790, 2.0223) 0.5712	0.5711	
Europe + Israel	166	23 (13.9)	143 (86.1)	NE (NE, NE)	81	9 (11.1)	72 (88.9)	NE (NE, NE)	0.9117 (0.4183, 1.9873) 0.8162	0.8185	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.6017
0	199	22 (11.1)	177 (88.9)	NE (NE, NE)	95	11 (11.6)	84 (88.4)	NE (NE, NE)	0.6298 (0.3018, 1.3143) 0.2180	0.2146	
1	172	21 (12.2)	151 (87.8)	NE (NE, NE)	77	8 (10.4)	69 (89.6)	NE (NE, NE)	0.8703 (0.3791, 1.9978) 0.7432	0.7439	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Vascular disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.0338
0	60	5 (8.3)	55 (91.7)	NE (NE, NE)	31	5 (16.1)	26 (83.9)	NE (NE, NE)	0.4245 (0.1223, 1.4737) 0.1772	0.1667	
1	107	8 (7.5)	99 (92.5)	NE (NE, NE)	48	8 (16.7)	40 (83.3)	NE (NE, NE)	0.3529 (0.1312, 0.9490) 0.0390	0.0312	
2	114	18 (15.8)	96 (84.2)	NE (NE, NE)	50	5 (10.0)	45 (90.0)	NE (NE, NE)	0.9684 (0.3513, 2.6694) 0.9505	0.9493	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	12 (13.3)	78 (86.7)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	3.9266 (0.5029, 30.6597) 0.1921	0.1600	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.3110
PD	173	19 (11.0)	154 (89.0)	NE (NE, NE)	77	9 (11.7)	68 (88.3)	NE (NE, NE)	0.6412 (0.2848, 1.4438)	0.2799	
PR	48	2 (4.2)	46 (95.8)	NE (NE, NE)	21	2 (9.5)	19 (90.5)	NE (NE, NE)	0.2832 (0.0362, 2.1570)	0.1945	
SD	82	13 (15.9)	69 (84.1)	NE (NE, NE)	54	5 (9.3)	49 (90.7)	NE (NE, NE)	0.2795 (0.0362, 2.1570)	0.6070	
									0.2215 (0.4636, 3.7191)		
									0.6080		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Vascular disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.0764
Yes	37	5 (13.5)	32 (86.5)	NE (11.8, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9962	0.2993	
No	334	38 (11.4)	296 (88.6)	NE (NE, NE)	159	19 (11.9)	140 (88.1)	NE (NE, NE)	0.6679 (0.3812, 1.1702) 0.1584	0.1561	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Vascular disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.6872
Yes	24	2 (8.3)	22 (91.7)	NE (11.4, NE)	7	1 (14.3)	6 (85.7)	NE (0.0, NE)	0.4441 (0.0393, 5.0132) 0.5116	0.5003	
No	347	41 (11.8)	306 (88.2)	NE (NE, NE)	165	18 (10.9)	147 (89.1)	NE (NE, NE)	0.7491 (0.4261, 1.3170) 0.3156	0.3142	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
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 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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SOC: Vascular disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0062
Normal Function	201	19 (9.5)	182 (90.5)	NE (NE, NE)	80	15 (18.8)	65 (81.3)	NE (NE, NE)	0.3394 (0.1695, 0.6795) 0.0023	0.0014	
Mild Impairment	123	17 (13.8)	106 (86.2)	NE (NE, NE)	65	3 (4.6)	62 (95.4)	NE (NE, NE)	1.8474 (0.5311, 6.4264) 0.3345	0.3276	
Moderate Impairment	41	5 (12.2)	36 (87.8)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	2.3267 (0.2712, 19.9651) 0.4413	0.4278	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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DE.T.4.8.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Vascular disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1479
Normal Function	170	20 (11.8)	150 (88.2)	NE (NE, NE)	88	7 (8.0)	81 (92.0)	NE (NE, NE)	1.0622 (0.4438, 2.5419) 0.8923	0.8931	
Mild Impairment	194	21 (10.8)	173 (89.2)	NE (NE, NE)	82	12 (14.6)	70 (85.4)	NE (NE, NE)	0.4640 (0.2238, 0.9618) 0.0390	0.0351	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.5420
Yes	331	39 (11.8)	292 (88.2)	NE (NE, NE)	146	16 (11.0)	130 (89.0)	NE (NE, NE)	0.7831 (0.4340, 1.4131) 0.4169	0.4159	
No	40	4 (10.0)	36 (90.0)	NE (NE, NE)	26	3 (11.5)	23 (88.5)	NE (NE, NE)	0.4016 (0.0818, 1.9724) 0.2612	0.2502	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.5589
Positive	329	36 (10.9)	293 (89.1)	NE (NE, NE)	152	15 (9.9)	137 (90.1)	NE (NE, NE)	0.7680 (0.4165, 1.4164) 0.3980	0.3962	
Negative	42	7 (16.7)	35 (83.3)	NE (15.5, NE)	20	4 (20.0)	16 (80.0)	NE (2.9, NE)	0.5732 (0.1601, 2.0519) 0.3924	0.3907	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.7299
Positive	331	36 (10.9)	295 (89.1)	NE (NE, NE)	155	17 (11.0)	138 (89.0)	NE (NE, NE)	0.7033 (0.3915, 1.2635)	0.2366	
Negative	40	7 (17.5)	33 (82.5)	NE (11.8, NE)	17	2 (11.8)	15 (88.2)	NE (NE, NE)	0.2390 (0.1585, 4.3195)	0.8219	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Hypertension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.9764
HER2 IHC 1+	214	8 (3.7)	206 (96.3)	NE (NE, NE)	100	4 (4.0)	96 (96.0)	NE (NE, NE)	0.8556 (0.2566, 2.8532) 0.7997	0.7987	
HER2 IHC 2+/ISH Negative	157	6 (3.8)	151 (96.2)	NE (NE, NE)	72	3 (4.2)	69 (95.8)	NE (NE, NE)	0.6542 (0.1590, 2.6924) 0.5566	0.5541	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Vascular disorders; PT: Hypertension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.0380
1	220	4 (1.8)	216 (98.2)	NE (NE, NE)	94	5 (5.3)	89 (94.7)	NE (NE, NE)	0.3229 (0.0866, 1.2036) 0.0922	0.0759	
>=2	150	10 (6.7)	140 (93.3)	NE (NE, NE)	78	2 (2.6)	76 (97.4)	NE (NE, NE)	1.8806 (0.4029, 8.7784) 0.4217	0.4139	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Hypertension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.7499
Yes	233	8 (3.4)	225 (96.6)	NE (NE, NE)	112	3 (2.7)	109 (97.3)	NE (NE, NE)	1.1577 (0.3060, 4.3808) 0.8292	0.8278	
No	98	4 (4.1)	94 (95.9)	NE (NE, NE)	43	2 (4.7)	41 (95.3)	NE (NE, NE)	0.7409 (0.1339, 4.0982) 0.7311	0.7302	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Vascular disorders; PT: Hypertension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5037
<65	289	11 (3.8)	278 (96.2)	NE (NE, NE)	126	6 (4.8)	120 (95.2)	NE (NE, NE)	0.6684 (0.2443, 1.8283) 0.4326	0.4304	
>=65	82	3 (3.7)	79 (96.3)	NE (NE, NE)	46	1 (2.2)	45 (97.8)	NE (NE, NE)	1.3391 (0.1359, 13.1905) 0.8025	0.8018	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Vascular disorders; PT: Hypertension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1862
<75	357	14 (3.9)	343 (96.1)	NE (NE, NE)	163	6 (3.7)	157 (96.3)	NE (NE, NE)	0.8606 (0.3264, 2.2689)	0.7615	0.7619
>=75	14	0	14 (100)	NE (NE, NE)	9	1 (11.1)	8 (88.9)	NE (0.7, NE)	0.0000 (0.0000, )	0.9984	0.2294

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Vascular disorders; PT: Hypertension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.9314
White	175	6 (3.4)	169 (96.6)	NE (NE, NE)	85	3 (3.5)	82 (96.5)	NE (NE, NE)	0.8329 (0.2069, 3.3530) 0.7970	0.7970	
Non-White	196	8 (4.1)	188 (95.9)	NE (NE, NE)	86	4 (4.7)	82 (95.3)	NE (NE, NE)	0.6855 (0.2016, 2.3309) 0.5453	0.5423	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Hypertension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.2272
Asia	147	3 (2.0)	144 (98.0)	NE (NE, NE)	63	3 (4.8)	60 (95.2)	NE (NE, NE)	0.2571 (0.0473, 1.3982) 0.1159	0.0941	
North America	58	2 (3.4)	56 (96.6)	NE (NE, NE)	28	2 (7.1)	26 (92.9)	NE (NE, NE)	0.4564 (0.0642, 3.2427) 0.4330	0.4213	
Europe + Israel	166	9 (5.4)	157 (94.6)	NE (NE, NE)	81	2 (2.5)	79 (97.5)	NE (NE, NE)	1.9521 (0.4204, 9.0643) 0.3932	0.3839	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Hypertension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.7413
0	199	7 (3.5)	192 (96.5)	NE (NE, NE)	95	4 (4.2)	91 (95.8)	NE (NE, NE)	0.6446 (0.1857, 2.2367) 0.4890	0.4871	
1	172	7 (4.1)	165 (95.9)	NE (NE, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	0.9149 (0.2324, 3.6021) 0.8987	0.8984	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Hypertension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.0013
0	60	1 (1.7)	59 (98.3)	NE (NE, NE)	31	4 (12.9)	27 (87.1)	NE (NE, NE)	0.1064 (0.0118, 0.9581)	0.0152	
1	107	0	107 (100)	NE (NE, NE)	48	2 (4.2)	46 (95.8)	NE (NE, NE)	0.0000 (0.0000, )	0.0343	
2	114	8 (7.0)	106 (93.0)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	0.9968 (NE, NE)	0.1023	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Hypertension

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 (5.6)	85 (94.4)	NE (NE, NE)	43 (2.3)	42 (97.7)	NE (NE, NE)	2.0372 (0.2329, 17.8168) 0.5201	0.5122	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Hypertension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.6006
PD	173	7 (4.0)	166 (96.0)	NE (NE, NE)	77	4 (5.2)	73 (94.8)	NE (NE, NE)	0.5848 (0.1660, 2.0601)	0.3999	
PR	48	1 (2.1)	47 (97.9)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	0.4037 (NE, NE)	0.5083	
SD	82	4 (4.9)	78 (95.1)	NE (NE, NE)	54	2 (3.7)	52 (96.3)	NE (NE, NE)	1.0375 (0.1841, 5.8480)	0.9660	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Hypertension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.4176
Yes	37	1 (2.7)	36 (97.3)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9982	0.6347	
No	334	13 (3.9)	321 (96.1)	NE (NE, NE)	159	7 (4.4)	152 (95.6)	NE (NE, NE)	0.7238 (0.2847, 1.8404) 0.4973	0.4958	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Vascular disorders; PT: Hypertension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0861
Yes	24	0	24 (100)	NE (NE, NE)	7	1 (14.3)	6 (85.7)	NE (0.0, NE)	0.0000 (0.0000, ) 0.9983	0.0641	
No	347	14 (4.0)	333 (96.0)	NE (NE, NE)	165	6 (3.6)	159 (96.4)	NE (NE, NE)	0.8986 (0.3408, 2.3695) 0.8289	0.8287	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Vascular disorders; PT: Hypertension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.8280
Normal Function	201	10 (5.0)	191 (95.0)	NE (NE, NE)	80	5 (6.3)	75 (93.8)	NE (NE, NE)	0.6975 (0.2373, 2.0507) 0.5127	0.5113	
Mild Impairment	123	3 (2.4)	120 (97.6)	NE (NE, NE)	65	1 (1.5)	64 (98.5)	NE (NE, NE)	0.8197 (0.0753, 8.9173) 0.8703	0.8701	
Moderate Impairment	41	1 (2.4)	40 (97.6)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	0.5116 (0.0320, 8.1861) 0.6357	0.6293	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Vascular disorders; PT: Hypertension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.2279
Normal Function	170	9 (5.3)	161 (94.7)	NE (NE, NE)	88	3 (3.4)	85 (96.6)	NE (NE, NE)	1.4286 (0.3854, 5.2947) 0.5936	0.5924	
Mild Impairment	194	5 (2.6)	189 (97.4)	NE (NE, NE)	82	4 (4.9)	78 (95.1)	NE (NE, NE)	0.3438 (0.0869, 1.3612) 0.1283	0.1132	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Vascular disorders; PT: Hypertension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.7227
Yes	331	13 (3.9)	318 (96.1)	NE (NE, NE)	146	6 (4.1)	140 (95.9)	NE (NE, NE)	0.7918 (0.2976, 2.1067) 0.6401	0.6393	
No	40	1 (2.5)	39 (97.5)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	0.5133 (0.0315, 8.3673) 0.6396	0.6336	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Hypertension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.4369
Positive	329	12 (3.6)	317 (96.4)	NE (NE, NE)	152	5 (3.3)	147 (96.7)	NE (NE, NE)	0.9636 (0.3371, 2.7542) 0.9449	0.9454	
Negative	42	2 (4.8)	40 (95.2)	NE (15.5, NE)	20	2 (10.0)	18 (90.0)	NE (NE, NE)	0.1829 (0.0161, 2.0810) 0.1709	0.1267	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Hypertension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.3606
Positive	331	12 (3.6)	319 (96.4)	NE (NE, NE)	155	5 (3.2)	150 (96.8)	NE (NE, NE)	0.9787 (0.3424, 2.7975)	0.9682	
Negative	40	2 (5.0)	38 (95.0)	NE (15.5, NE)	17	2 (11.8)	15 (88.2)	NE (NE, NE)	0.1495 (0.0128, 1.7407)	0.0839	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Injury, poisoning and procedural complications; PT: Fall

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0950
HER2 IHC 1+	214	7 (3.3)	207 (96.7)	NE (NE, NE)	100	0	100 (100)	NE (NE, NE)	NE (NE, NE) 0.9930	0.2192	
HER2 IHC 2+/ISH Negative	157	6 (3.8)	151 (96.2)	NE (NE, NE)	72	2 (2.8)	70 (97.2)	NE (NE, NE)	0.7836 (0.1521, 4.0370) 0.7707	0.7702	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Fall

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.0620
1	220	5 (2.3)	215 (97.7)	NE (NE, NE)	94	2 (2.1)	92 (97.9)	NE (NE, NE)	0.6980 (0.1327, 3.6731) 0.6713	0.6700	
>=2	150	8 (5.3)	142 (94.7)	NE (NE, NE)	78	0	78 (100)	NE (NE, NE)	NE (NE, NE) 0.9927	0.1988	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Fall

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.2964
Yes	233	10 (4.3)	223 (95.7)	NE (NE, NE)	112	2 (1.8)	110 (98.2)	NE (NE, NE)	1.2617 (0.2670, 5.9632) 0.7693	0.7687	
No	98	3 (3.1)	95 (96.9)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9970	0.4139	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:37; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_AESOCPT10PAT\_2\_SAS.rf

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SOC: Injury, poisoning and procedural complications; PT: Fall

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1690
<65	289	7 (2.4)	282 (97.6)	NE (NE, NE)	126	0	126 (100)	NE (NE, NE)	NE (NE, NE) 0.9931	0.2166	
>=65	82	6 (7.3)	76 (92.7)	NE (NE, NE)	46	2 (4.3)	44 (95.7)	NE (NE, NE)	1.0349 (0.2042, 5.2438) 0.9670	0.9667	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Fall

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3940
<75	357	12 (3.4)	345 (96.6)	NE (NE, NE)	163	2 (1.2)	161 (98.8)	NE (NE, NE)	1.3281 (0.2882, 6.1206) 0.7159	0.7149	
>=75	14	1 (7.1)	13 (92.9)	NE (5.1, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9985	0.4795	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Injury, poisoning and procedural complications; PT: Fall

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.1802
White	175	8 (4.6)	167 (95.4)	NE (NE, NE)	85	2 (2.4)	83 (97.6)	NE (NE, NE)	1.0336 (0.2116, 5.0495) 0.9675	0.9672	
Non-White	196	5 (2.6)	191 (97.4)	NE (NE, NE)	86	0	86 (100)	NE (NE, NE)	NE (NE, NE) 0.9943	0.3235	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Fall

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.2206
Asia	147	2 (1.4)	145 (98.6)	NE (NE, NE)	63	0	63 (100)	NE (NE, NE)	NE (NE, NE) 0.9965	0.5608	
North America	58	6 (10.3)	52 (89.7)	NE (NE, NE)	28	2 (7.1)	26 (92.9)	NE (NE, NE)	0.7068 (0.1326, 3.7683) 0.6845	0.6833	
Europe + Israel	166	5 (3.0)	161 (97.0)	NE (NE, NE)	81	0	81 (100)	NE (NE, NE)	NE (NE, NE) 0.9961	0.2805	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Injury, poisoning and procedural complications; PT: Fall

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.0394
0	199	9 (4.5)	190 (95.5)	NE (NE, NE)	95	0	95 (100)	NE (NE, NE)	NE (NE, NE) 0.9945	0.1256	
1	172	4 (2.3)	168 (97.7)	NE (NE, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	0.3700 (0.0618, 2.2145) 0.2761	0.2602	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Fall

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.3409
0	60	0	60 (100)	NE (NE, NE)	31	0	31 (100)	NE (NE, NE)	NE (NE, NE)		
1	107	3 (2.8)	104 (97.2)	NE (NE, NE)	48	0	48 (100)	NE (NE, NE)	NE (NE, NE)	0.3569	
2	114	6 (5.3)	108 (94.7)	NE (NE, NE)	50	2 (4.0)	48 (96.0)	NE (NE, NE)	0.9967 0.7612 (0.1468, 3.9469) 0.7452	0.7446	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Fall

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	4 (4.4)	86 (95.6)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9959	0.4983	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Injury, poisoning and procedural complications; PT: Fall

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.8024
PD	173	9 (5.2)	164 (94.8)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	1.9573 (0.2389, 16.0332)	0.5241	
PR	48	1 (2.1)	47 (97.9)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	NE (NE, NE) 0.9979	0.7353	
SD	82	1 (1.2)	81 (98.8)	NE (NE, NE)	54	0	54 (100)	NE (NE, NE)	NE (NE, NE) 0.9977	0.4497	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Injury, poisoning and procedural complications; PT: Fall

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.1050
Yes	37	1 (2.7)	36 (97.3)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	0.3422 (0.0214, 5.4726)	0.4266	
No	334	12 (3.6)	322 (96.4)	NE (NE, NE)	159	1 (0.6)	158 (99.4)	NE (NE, NE)	0.4484 (0.3352, 20.4487)	0.3408	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Fall

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.9999
Yes	24	0	24 (100)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE)		
No	347	13 (3.7)	334 (96.3)	NE (NE, NE)	165	2 (1.2)	163 (98.8)	NE (NE, NE)	1.5611 (0.3442, 7.0804) 0.5637	0.5606	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Fall

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.2693
Normal Function	201	6 (3.0)	195 (97.0)	NE (NE, NE)	80	0	80 (100)	NE (NE, NE)	NE (NE, NE) 0.9936	0.2521	
Mild Impairment	123	3 (2.4)	120 (97.6)	NE (NE, NE)	65	0	65 (100)	NE (NE, NE)	NE (NE, NE) 0.9968	0.3770	
Moderate Impairment	41	4 (9.8)	37 (90.2)	NE (NE, NE)	23	2 (8.7)	21 (91.3)	NE (NE, NE)	0.8876 (0.1614, 4.8800) 0.8909	0.8909	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Injury, poisoning and procedural complications; PT: Fall

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.7828
Normal Function	170	7 (4.1)	163 (95.9)	NE (NE, NE)	88	1 (1.1)	87 (98.9)	NE (NE, NE)	2.1787 (0.2649, 17.9196) 0.4689	0.4579	
Mild Impairment	194	6 (3.1)	188 (96.9)	NE (NE, NE)	82	1 (1.2)	81 (98.8)	NE (NE, NE)	1.0480 (0.1173, 9.3658) 0.9665	0.9665	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Fall

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1441
Yes	331	12 (3.6)	319 (96.4)	NE (NE, NE)	146	1 (0.7)	145 (99.3)	NE (NE, NE)	2.8545 (0.3651, 22.3204) 0.3175	0.2961	
No	40	1 (2.5)	39 (97.5)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	0.2599 (0.0149, 4.5482) 0.3562	0.3253	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Injury, poisoning and procedural complications; PT: Fall

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.9999
Positive	329	13 (4.0)	316 (96.0)	NE (NE, NE)	152	2 (1.3)	150 (98.7)	NE (NE, NE)	1.5808 (0.3498, 7.1436)	0.5485	
Negative	42	0	42 (100)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Fall

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.9999
Positive	331	13 (3.9)	318 (96.1)	NE (NE, NE)	155	2 (1.3)	153 (98.7)	NE (NE, NE)	1.5981 (0.3534, 7.2272)	0.5391	
Negative	40	0	40 (100)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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SOC: Injury, poisoning and procedural complications; PT: Medication error

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.9998
HER2 IHC 1+	214	0	214 (100)	NE (NE, NE)	100	7 (7.0)	93 (93.0)	NE (NE, NE)	0.0000 (0.0000, ) 0.9940	<0.0001	
HER2 IHC 2+/ISH Negative	157	0	157 (100)	NE (NE, NE)	72	4 (5.6)	68 (94.4)	NE (NE, NE)	0.0000 (0.0000, ) 0.9955	0.0029	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.8.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Injury, poisoning and procedural complications; PT: Medication error

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											1.0000
1	220	0	220 (100)	NE (NE, NE)	94	6 (6.4)	88 (93.6)	NE (NE, NE)	0.0000 (0.0000, ) 0.9947	0.0002	
>=2	150	0	150 (100)	NE (NE, NE)	78	5 (6.4)	73 (93.6)	NE (NE, NE)	0.0000 (0.0000, ) 0.9947	0.0018	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Injury, poisoning and procedural complications; PT: Medication error

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.9997
Yes	233	0	233 (100)	NE (NE, NE)	112	4 (3.6)	108 (96.4)	NE (NE, NE)	0.0000 (0.0000, ) 0.9954	0.0038	
No	98	0	98 (100)	NE (NE, NE)	43	7 (16.3)	36 (83.7)	NE (NE, NE)	0.0000 (0.0000, ) 0.9943	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Medication error

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9998
<65	289	0	289 (100)	NE (NE, NE)	126	10 (7.9)	116 (92.1)	NE (NE, NE)	0.0000 (0.0000, ) 0.9931	<0.0001	
>=65	82	0	82 (100)	NE (NE, NE)	46	1 (2.2)	45 (97.8)	NE (NE, NE)	0.0000 (0.0000, ) 0.9976	0.1818	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Medication error

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9997
<75	357	0	357 (100)	NE (NE, NE)	163	11 (6.7)	152 (93.3)	NE (NE, NE)	0.0000 (0.0000, ) 0.9926	<0.0001	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Medication error

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.9998
White	175	0	175 (100)	NE (NE, NE)	85	0	85 (100)	NE (NE, NE)	NE (NE, NE)		
Non-White	196	0	196 (100)	NE (NE, NE)	86	11 (12.8)	75 (87.2)	NE (NE, NE)	0.0000 (0.0000, ) 0.9928	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Medication error

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											1.0000
Asia	147	0	147 (100)	NE (NE, NE)	63	11 (17.5)	52 (82.5)	NE (NE, NE)	0.0000 (0.0000, ) 0.9930	<0.0001	
North America	58	0	58 (100)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE)		
Europe + Israel	166	0	166 (100)	NE (NE, NE)	81	0	81 (100)	NE (NE, NE)	NE (NE, NE)		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Medication error

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											1.0000
0	199	0	199 (100)	NE (NE, NE)	95	6 (6.3)	89 (93.7)	NE (NE, NE)	0.0000 (0.0000, ) 0.9944	0.0003	
1	172	0	172 (100)	NE (NE, NE)	77	5 (6.5)	72 (93.5)	NE (NE, NE)	0.0000 (0.0000, ) 0.9950	0.0008	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Medication error

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											1.0000
0	60	0	60 (100)	NE (NE, NE)	31	3 (9.7)	28 (90.3)	NE (NE, NE)	0.0000 (0.0000, ) 0.9959	0.0148	
1	107	0	107 (100)	NE (NE, NE)	48	5 (10.4)	43 (89.6)	NE (NE, NE)	0.0000 (0.0000, ) 0.9951	0.0007	
2	114	0	114 (100)	NE (NE, NE)	50	1 (2.0)	49 (98.0)	NE (NE, NE)	0.0000 (0.0000, ) 0.9978	0.1311	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Medication error

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	0	90 (100)	NE (NE, NE)	43	2 (4.7)	41 (95.3)	NE (NE, NE)	0.0000 (0.0000, ) 0.9968	0.0400	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Medication error

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											1.0000
PD	173	0	173 (100)	NE (NE, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	0.0000 (0.0000, ) 0.9961	0.0091	
PR	48	0	48 (100)	NE (NE, NE)	21	2 (9.5)	19 (90.5)	NE (NE, NE)	0.0000 (0.0000, ) 0.9969	0.0312	
SD	82	0	82 (100)	NE (NE, NE)	54	2 (3.7)	52 (96.3)	NE (NE, NE)	0.0000 (0.0000, ) 0.9965	0.0803	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.8.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Injury, poisoning and procedural complications; PT: Medication error

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.9996
Yes	37	0	37 (100)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE)	NE	
No	334	0	334 (100)	NE (NE, NE)	159	11 (6.9)	148 (93.1)	NE (NE, NE)	0.0000 (0.0000, ) 0.9925	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Medication error

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.9997
Yes	24	0	24 (100)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE)		
No	347	0	347 (100)	NE (NE, NE)	165	11 (6.7)	154 (93.3)	NE (NE, NE)	0.0000 (0.0000, ) 0.9925	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Medication error

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											NE
Normal Function	201	0	201 (100)	NE (NE, NE)	80	8 (10.0)	72 (90.0)	NE (NE, NE)	0.0000 (0.0000, ) 0.9941	<0.0001	
Mild Impairment	123	0	123 (100)	NE (NE, NE)	65	3 (4.6)	62 (95.4)	NE (NE, NE)	0.0000 (0.0000, ) 0.9959	0.0166	
Moderate Impairment	41	0	41 (100)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Medication error

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											NE
Normal Function	170	0	170 (100)	NE (NE, NE)	88	8 (9.1)	80 (90.9)	NE (NE, NE)	0.0000 (0.0000, ) 0.9934	<0.0001	
Mild Impairment	194	0	194 (100)	NE (NE, NE)	82	3 (3.7)	79 (96.3)	NE (NE, NE)	0.0000 (0.0000, ) 0.9962	0.0075	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Medication error

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.9996
Yes	331	0	331 (100)	NE (NE, NE)	146	8 (5.5)	138 (94.5)	NE (NE, NE)	0.0000 (0.0000, ) 0.9937	<0.0001	
No	40	0	40 (100)	NE (NE, NE)	26	3 (11.5)	23 (88.5)	NE (NE, NE)	0.0000 (0.0000, ) 0.9973	0.0291	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Medication error

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											NE
Positive	329	0	329 (100)	NE (NE, NE)	152	11 (7.2)	141 (92.8)	NE (NE, NE)	0.0000 (0.0000, ) 0.9925	<0.0001	
Negative	42	0	42 (100)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Medication error

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											NE
Positive	331	0	331 (100)	NE (NE, NE)	155	11 (7.1)	144 (92.9)	NE (NE, NE)	0.0000 (0.0000, ) 0.9925	<0.0001	
Negative	40	0	40 (100)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Contusion

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.3965
HER2 IHC 1+	214	7 (3.3)	207 (96.7)	NE (NE, NE)	100	1 (1.0)	99 (99.0)	NE (NE, NE)	1.6971 (0.1977, 14.5646) 0.6296	0.6258	
HER2 IHC 2+/ISH Negative	157	3 (1.9)	154 (98.1)	NE (NE, NE)	72	0	72 (100)	NE (NE, NE)	NE (NE, NE) 0.9961	0.5192	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Hypotension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.2547
HER2 IHC 1+	214	5 (2.3)	209 (97.7)	NE (NE, NE)	100	1 (1.0)	99 (99.0)	NE (NE, NE)	1.8633 (0.2140, 16.2245) 0.5730	0.5670	
HER2 IHC 2+/ISH Negative	157	5 (3.2)	152 (96.8)	NE (NE, NE)	72	0	72 (100)	NE (NE, NE)	NE (NE, NE) 0.9953	0.1594	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Contusion

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.1847
1	220	6 (2.7)	214 (97.3)	NE (NE, NE)	94	0	94 (100)	NE (NE, NE)	NE (NE, NE) 0.9959	0.2427	
>=2	150	4 (2.7)	146 (97.3)	NE (NE, NE)	78	1 (1.3)	77 (98.7)	NE (NE, NE)	0.6535 (0.0622, 6.8634) 0.7230	0.7216	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Hypotension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.0768
1	220	2 (0.9)	218 (99.1)	NE (NE, NE)	94	1 (1.1)	93 (98.9)	NE (NE, NE)	0.5970 (0.0518, 6.8761) 0.6791	0.6760	
>=2	150	8 (5.3)	142 (94.7)	NE (NE, NE)	78	0	78 (100)	NE (NE, NE)	NE (NE, NE) 0.9938	0.0580	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Contusion

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.4889
Yes	233	7 (3.0)	226 (97.0)	NE (NE, NE)	112	1 (0.9)	111 (99.1)	NE (NE, NE)	1.6409 (0.1930, 13.9534) 0.6502	0.6471	
No	98	2 (2.0)	96 (98.0)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9969	0.5659	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Hypotension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.6205
Yes	233	7 (3.0)	226 (97.0)	NE (NE, NE)	112	1 (0.9)	111 (99.1)	NE (NE, NE)	2.6054 (0.3158, 21.4926) 0.3738	0.3560	
No	98	1 (1.0)	97 (99.0)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9978	0.5077	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:37; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_AESOCPT10PAT\_2\_SAS.rtf

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SOC: Injury, poisoning and procedural complications; PT: Contusion

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2608
<65	289	6 (2.1)	283 (97.9)	NE (NE, NE)	126	0	126 (100)	NE (NE, NE)	NE (NE, NE) 0.9936	0.2527	
>=65	82	4 (4.9)	78 (95.1)	NE (17.4, NE)	46	1 (2.2)	45 (97.8)	NE (NE, NE)	0.6373 (0.0503, 8.0821) 0.7282	0.7263	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Vascular disorders; PT: Hypotension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4532
<65	289	8 (2.8)	281 (97.2)	NE (NE, NE)	126	1 (0.8)	125 (99.2)	NE (NE, NE)	2.9023 (0.3598, 23.4105) 0.3171	0.2947	
>=65	82	2 (2.4)	80 (97.6)	NE (NE, NE)	46	0	46 (100)	NE (NE, NE)	NE (NE, NE) 0.9969	0.3406	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Injury, poisoning and procedural complications; PT: Contusion

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4663
<75	357	9 (2.5)	348 (97.5)	NE (NE, NE)	163	1 (0.6)	162 (99.4)	NE (NE, NE)	1.6830 (0.2016, 14.0516) 0.6307	0.6271	
>=75	14	1 (7.1)	13 (92.9)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9985	0.4142	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Vascular disorders; PT: Hypotension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9998
<75	357	10 (2.8)	347 (97.2)	NE (NE, NE)	163	1 (0.6)	162 (99.4)	NE (NE, NE)	3.7709 (0.4793, 29.6668) 0.2072	0.1756	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Contusion

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.2485
White	175	5 (2.9)	170 (97.1)	NE (NE, NE)	85	0	85 (100)	NE (NE, NE)	NE (NE, NE) 0.9958	0.2321	
Non-White	196	5 (2.6)	191 (97.4)	NE (NE, NE)	86	1 (1.2)	85 (98.8)	NE (NE, NE)	0.7368 (0.0768, 7.0635) 0.7911	0.7905	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Vascular disorders; PT: Hypotension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.6659
White	175	9 (5.1)	166 (94.9)	NE (NE, NE)	85	1 (1.2)	84 (98.8)	NE (NE, NE)	3.5051 (0.4405, 27.8910) 0.2359	0.2064	
Non-White	196	1 (0.5)	195 (99.5)	NE (NE, NE)	86	0	86 (100)	NE (NE, NE)	NE (NE, NE) 0.9978	0.5077	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Injury, poisoning and procedural complications; PT: Contusion

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.5061
Asia	147	5 (3.4)	142 (96.6)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (NE, NE)	0.7114 (0.0750, 6.7497) 0.7667	0.7660	
North America	58	3 (5.2)	55 (94.8)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9968	0.3465	
Europe + Israel	166	2 (1.2)	164 (98.8)	NE (NE, NE)	81	0	81 (100)	NE (NE, NE)	NE (NE, NE) 0.9974	0.4715	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Vascular disorders; PT: Hypotension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.5278
Asia	147	0	147 (100)	NE (NE, NE)	63	0	63 (100)	NE (NE, NE)	NE (NE, NE)		
North America	58	5 (8.6)	53 (91.4)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9951	0.1362	
Europe + Israel	166	5 (3.0)	161 (97.0)	NE (NE, NE)	81	1 (1.2)	80 (98.8)	NE (NE, NE)	1.8431 (0.2111, 16.0950) 0.5802	0.5745	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Contusion

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.1467
0	199	7 (3.5)	192 (96.5)	NE (NE, NE)	95	0	95 (100)	NE (NE, NE)	NE (NE, NE) 0.9936	0.2525	
1	172	3 (1.7)	169 (98.3)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	0.7378 (0.0667, 8.1612) 0.8042	0.8035	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Hypotension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.2536
0	199	5 (2.5)	194 (97.5)	NE (NE, NE)	95	1 (1.1)	94 (98.9)	NE (NE, NE)	1.8654 (0.2136, 16.2916) 0.5729	0.5668	
1	172	5 (2.9)	167 (97.1)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE) 0.9952	0.1485	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Contusion

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.3222
0	60	2 (3.3)	58 (96.7)	NE (17.4, NE)	31	0	31 (100)	NE (NE, NE)	NE (NE, NE) 0.9972	0.4142	
1	107	3 (2.8)	104 (97.2)	NE (NE, NE)	48	0	48 (100)	NE (NE, NE)	NE (NE, NE) 0.9970	0.4254	
2	114	3 (2.6)	111 (97.4)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	NE (NE, NE) 0.9964	0.3021	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Contusion

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	2 (2.2)	88 (97.8)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	0.2116 (0.0113, 3.9497) 0.2983	0.2612	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Hypotension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.4278
0	60	2 (3.3)	58 (96.7)	NE (NE, NE)	31	0	31 (100)	NE (NE, NE)	NE (NE, NE) 0.9968	0.3073	
1	107	2 (1.9)	105 (98.1)	NE (NE, NE)	48	1 (2.1)	47 (97.9)	NE (NE, NE)	0.8701 (0.0789, 9.6018) 0.9096	0.9095	
2	114	4 (3.5)	110 (96.5)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	NE (NE, NE) 0.9962	0.2756	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Hypotension

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2)											
>=3	90	2 (2.2)	88 (97.8)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9971	0.4005	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Contusion

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.5126
PD	173	5 (2.9)	168 (97.1)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE) 0.9961	0.2762	
PR	48	0	48 (100)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	NE (NE, NE) NE		
SD	82	3 (3.7)	79 (96.3)	NE (19.7, NE)	54	1 (1.9)	53 (98.1)	NE (NE, NE)	0.6051 (0.0506, 7.2378) 0.6915	0.6892	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Hypotension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.5495
PD	173	5 (2.9)	168 (97.1)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	1.8335 (0.2106, 15.9660)	0.5774	
PR	48	0	48 (100)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	NE (NE, NE)		
SD	82	3 (3.7)	79 (96.3)	NE (NE, NE)	54	0	54 (100)	NE (NE, NE)	NE (NE, NE) 0.9960	0.1954	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Contusion

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.6941
Yes	37	1 (2.7)	36 (97.3)	NE (17.4, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE)	NE	
No	334	9 (2.7)	325 (97.3)	NE (NE, NE)	159	1 (0.6)	158 (99.4)	NE (NE, NE)	2.0846 (0.2535, 17.1453)	0.4851	0.4944

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Hypotension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.7012
Yes	37	1 (2.7)	36 (97.3)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9981	0.5876	
No	334	9 (2.7)	325 (97.3)	NE (NE, NE)	159	1 (0.6)	158 (99.4)	NE (NE, NE)	3.5512 (0.4466, 28.2394) 0.2309	0.2009	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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DE.T.4.8.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Injury, poisoning and procedural complications; PT: Contusion

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.5236
Yes	24	2 (8.3)	22 (91.7)	17.4 (17.4, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9985	0.6949	
No	347	8 (2.3)	339 (97.7)	NE (NE, NE)	165	1 (0.6)	164 (99.4)	NE (NE, NE)	1.8908 (0.2259, 15.8283) 0.5568	0.5504	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Hypotension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.9998
Yes	24	0	24 (100)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE)		
No	347	10 (2.9)	337 (97.1)	NE (NE, NE)	165	1 (0.6)	164 (99.4)	NE (NE, NE)	3.9395 (0.5008, 30.9882) 0.1926	0.1598	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Contusion

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											1.0000
Normal Function	201	5 (2.5)	196 (97.5)	NE (NE, NE)	80	0	80 (100)	NE (NE, NE)	NE (NE, NE) 0.9962	0.5450	
Mild Impairment	123	2 (1.6)	121 (98.4)	NE (NE, NE)	65	0	65 (100)	NE (NE, NE)	NE (NE, NE) 0.9971	0.3981	
Moderate Impairment	41	3 (7.3)	38 (92.7)	NE (16.2, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9962	0.2359	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Hypotension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.2028
Normal Function	201	2 (1.0)	199 (99.0)	NE (NE, NE)	80	1 (1.3)	79 (98.8)	NE (NE, NE)	0.7201 (0.0650, 7.9825) 0.7890	0.7882	
Mild Impairment	123	5 (4.1)	118 (95.9)	NE (NE, NE)	65	0	65 (100)	NE (NE, NE)	NE (NE, NE) 0.9951	0.1304	
Moderate Impairment	41	2 (4.9)	39 (95.1)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9969	0.3462	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Contusion

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.2946
Normal Function	170	5 (2.9)	165 (97.1)	NE (NE, NE)	88	1 (1.1)	87 (98.9)	NE (NE, NE)	0.9122 (0.0940, 8.8525) 0.9368	0.9368	
Mild Impairment	194	5 (2.6)	189 (97.4)	NE (NE, NE)	82	0	82 (100)	NE (NE, NE)	NE (NE, NE) 0.9961	0.2802	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Hypotension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.5999
Normal Function	170	1 (0.6)	169 (99.4)	NE (NE, NE)	88	0	88 (100)	NE (NE, NE)	NE (NE, NE) 0.9978	0.4903	
Mild Impairment	194	8 (4.1)	186 (95.9)	NE (NE, NE)	82	1 (1.2)	81 (98.8)	NE (NE, NE)	2.6238 (0.3242, 21.2361) 0.3659	0.3477	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Contusion

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.5428
Yes	331	8 (2.4)	323 (97.6)	NE (NE, NE)	146	1 (0.7)	145 (99.3)	NE (NE, NE)	1.4990 (0.1771, 12.6914) 0.7103	0.7085	
No	40	2 (5.0)	38 (95.0)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9972	0.4242	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Vascular disorders; PT: Hypotension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.6138
Yes	331	9 (2.7)	322 (97.3)	NE (NE, NE)	146	1 (0.7)	145 (99.3)	NE (NE, NE)	3.4745 (0.4382, 27.5496) 0.2384	0.2090	
No	40	1 (2.5)	39 (97.5)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9982	0.6121	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Injury, poisoning and procedural complications; PT: Contusion

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.6677
Positive	329	9 (2.7)	320 (97.3)	NE (NE, NE)	152	1 (0.7)	151 (99.3)	NE (NE, NE)	2.0602 (0.2518, 16.8534)	0.4913	
Negative	42	1 (2.4)	41 (97.6)	NE (17.4, NE)	20	0	20 (100)	NE (NE, NE)	0.5003 (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Vascular disorders; PT: Hypotension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.3988
Positive	329	7 (2.1)	322 (97.9)	NE (NE, NE)	152	1 (0.7)	151 (99.3)	NE (NE, NE)	2.5786 (0.3139, 21.1836) 0.3780	0.3606	
Negative	42	3 (7.1)	39 (92.9)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) 0.9962	0.2419	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Contusion

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.6863
Positive	331	9 (2.7)	322 (97.3)	NE (NE, NE)	155	1 (0.6)	154 (99.4)	NE (NE, NE)	2.0912 (0.2554, 17.1247)	0.4822	
Negative	40	1 (2.5)	39 (97.5)	NE (17.4, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Vascular disorders; PT: Hypotension

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (derived)											0.5395
Positive	331	8 (2.4)	323 (97.6)	NE (NE, NE)	155	1 (0.6)	154 (99.4)	NE (NE, NE)	3.0926 (0.3836, 24.9345)	0.2642	
Negative	40	2 (5.0)	38 (95.0)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	0.2891 (NE, NE) 0.9971	0.3909	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Cardiac disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.1643
HER2 IHC 1+	214	16 (7.5)	198 (92.5)	NE (NE, NE)	100	8 (8.0)	92 (92.0)	NE (NE, NE)	0.5792 (0.2407, 1.3937) 0.2229	0.2175
HER2 IHC 2+/ISH Negative	157	19 (12.1)	138 (87.9)	NE (NE, NE)	72	4 (5.6)	68 (94.4)	NE (NE, NE)	1.4205 (0.4760, 4.2391) 0.5292	0.5262

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Cardiac disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.2442
1	220	21 (9.5)	199 (90.5)	NE (NE, NE)	94	9 (9.6)	85 (90.4)	NE (NE, NE)	0.6668 (0.3001, 1.4817) 0.3198	0.3173	
>=2	150	14 (9.3)	136 (90.7)	NE (NE, NE)	78	3 (3.8)	75 (96.2)	NE (NE, NE)	1.3991 (0.3908, 5.0096) 0.6058	0.6040	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Cardiac disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.2080
Yes	233	12 (5.2)	221 (94.8)	NE (NE, NE)	112	6 (5.4)	106 (94.6)	NE (NE, NE)	0.6174 (0.2248, 1.6961) 0.3497	0.3464	
No	98	15 (15.3)	83 (84.7)	NE (NE, NE)	43	3 (7.0)	40 (93.0)	NE (NE, NE)	1.5327 (0.4394, 5.3460) 0.5029	0.5003	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Cardiac disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8313
<65	289	25 (8.7)	264 (91.3)	NE (NE, NE)	126	8 (6.3)	118 (93.7)	NE (NE, NE)	0.8236 (0.3636, 1.8658) 0.6419	0.6421	
>=65	82	10 (12.2)	72 (87.8)	NE (NE, NE)	46	4 (8.7)	42 (91.3)	NE (NE, NE)	0.9497 (0.2897, 3.1132) 0.9322	0.9307	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Cardiac disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6613
<75	357	33 (9.2)	324 (90.8)	NE (NE, NE)	163	10 (6.1)	153 (93.9)	NE (NE, NE)	0.9263 (0.4481, 1.9147) 0.8362	0.8363	
>=75	14	2 (14.3)	12 (85.7)	NE (8.4, NE)	9	2 (22.2)	7 (77.8)	NE (2.6, NE)	0.5946 (0.0835, 4.2342) 0.6038	0.5997	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Cardiac disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.0479
White	175	12 (6.9)	163 (93.1)	NE (NE, NE)	85	8 (9.4)	77 (90.6)	NE (NE, NE)	0.4421 (0.1746, 1.1194) 0.0851	0.0776	
Non-White	196	23 (11.7)	173 (88.3)	NE (NE, NE)	86	4 (4.7)	82 (95.3)	NE (NE, NE)	1.6573 (0.5649, 4.8621) 0.3576	0.3534	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Cardiac disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.1323
Asia	147	20 (13.6)	127 (86.4)	NE (NE, NE)	63	3 (4.8)	60 (95.2)	NE (NE, NE)	1.8142 (0.5301, 6.2089) 0.3427	0.3367	
North America	58	5 (8.6)	53 (91.4)	NE (NE, NE)	28	4 (14.3)	24 (85.7)	NE (NE, NE)	0.2921 (0.0651, 1.3102) 0.1080	0.0875	
Europe + Israel	166	10 (6.0)	156 (94.0)	NE (NE, NE)	81	5 (6.2)	76 (93.8)	NE (NE, NE)	0.6574 (0.2191, 1.9724) 0.4543	0.4524	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Cardiac disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											
0	199	16 (8.0)	183 (92.0)	NE (NE, NE)	95	5 (5.3)	90 (94.7)	NE (NE, NE)	0.9650 (0.3465, 2.6875) 0.9457	0.9476	0.8366
1	172	19 (11.0)	153 (89.0)	NE (NE, NE)	77	7 (9.1)	70 (90.9)	NE (NE, NE)	0.7800 (0.3194, 1.9045) 0.5853	0.5842	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Cardiac disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.4346
0	60	6 (10.0)	54 (90.0)	NE (13.1, NE)	31	4 (12.9)	27 (87.1)	NE (NE, NE)	0.4739 (0.1261, 1.7810) 0.2689	0.2574	
1	107	12 (11.2)	95 (88.8)	NE (NE, NE)	48	3 (6.3)	45 (93.8)	NE (NE, NE)	1.4619 (0.4096, 5.2177) 0.5585	0.5559	
2	114	12 (10.5)	102 (89.5)	NE (NE, NE)	50	2 (4.0)	48 (96.0)	NE (NE, NE)	1.2880 (0.2746, 6.0424) 0.7482	0.7475	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Cardiac disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 (5.6)	85 (94.4)	NE (NE, NE)	43 (7.0)	40 (93.0)	NE (NE, NE)	0.4709 (0.1050, 2.1130) 0.3255	0.3177	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Cardiac disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.6109
PD	173	17 (9.8)	156 (90.2)	NE (NE, NE)	77	5 (6.5)	72 (93.5)	NE (NE, NE)	0.9234 (0.3305, 2.5801)	0.8791	
PR	48	2 (4.2)	46 (95.8)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	NE (NE, NE) 0.9972	0.6475	
SD	82	11 (13.4)	71 (86.6)	NE (NE, NE)	54	6 (11.1)	48 (88.9)	NE (NE, NE)	0.9336 (0.3412, 2.5547) 0.8935	0.8928	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Cardiac disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.6837
Yes	37	5 (13.5)	32 (86.5)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (2.1, NE)	1.2048 (0.1374, 10.5669)	0.8662	
No	334	30 (9.0)	304 (91.0)	NE (NE, NE)	159	11 (6.9)	148 (93.1)	NE (NE, NE)	0.8054 (0.3961, 1.6377)	0.5495	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Cardiac disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.8019
Yes	24	4 (16.7)	20 (83.3)	NE (NE, NE)	7	1 (14.3)	6 (85.7)	NE (2.1, NE)	1.2229 (0.1353, 11.0535) 0.8579	0.8576
No	347	31 (8.9)	316 (91.1)	NE (NE, NE)	165	11 (6.7)	154 (93.3)	NE (NE, NE)	0.8043 (0.3966, 1.6310) 0.5461	0.5457

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Cardiac disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.0716
Normal Function	201	17 (8.5)	184 (91.5)	NE (NE, NE)	80	8 (10.0)	72 (90.0)	NE (NE, NE)	0.6267 (0.2668, 1.4722) 0.2836	0.2799	
Mild Impairment	123	16 (13.0)	107 (87.0)	NE (NE, NE)	65	2 (3.1)	63 (96.9)	NE (NE, NE)	1.9755 (0.4364, 8.9431) 0.3769	0.3680	
Moderate Impairment	41	1 (2.4)	40 (97.6)	NE (NE, NE)	23	2 (8.7)	21 (91.3)	NE (NE, NE)	0.2502 (0.0226, 2.7644) 0.2583	0.2215	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Cardiac disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Hepatic function at baseline											
Normal Function	170	14 (8.2)	156 (91.8)	NE (NE, NE)	88	7 (8.0)	81 (92.0)	NE (NE, NE)	0.6074 (0.2389, 1.5445) 0.2951	0.2907	0.4233
Mild Impairment	194	21 (10.8)	173 (89.2)	NE (NE, NE)	82	5 (6.1)	77 (93.9)	NE (NE, NE)	1.1612 (0.4295, 3.1396) 0.7684	0.7683	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Cardiac disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.4057
Yes	331	29 (8.8)	302 (91.2)	NE (NE, NE)	146	11 (7.5)	135 (92.5)	NE (NE, NE)	0.7893 (0.3894, 1.5998) 0.5116	0.5108	
No	40	6 (15.0)	34 (85.0)	NE (13.1, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	1.5460 (0.1608, 14.8646) 0.7060	0.7039	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Cardiac disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.6836
Positive	329	28 (8.5)	301 (91.5)	NE (NE, NE)	152	9 (5.9)	143 (94.1)	NE (NE, NE)	0.9142 (0.4249, 1.9670) 0.8186	0.8190	
Negative	42	7 (16.7)	35 (83.3)	NE (15.5, NE)	20	3 (15.0)	17 (85.0)	NE (3.0, NE)	0.5747 (0.1280, 2.5807) 0.4698	0.4603	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Cardiac disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.6868
Positive	331	27 (8.2)	304 (91.8)	NE (NE, NE)	155	9 (5.8)	146 (94.2)	NE (NE, NE)	0.8840 (0.4089, 1.9110)	0.7543	
Negative	40	8 (20.0)	32 (80.0)	15.5 (8.4, NE)	17	3 (17.6)	14 (82.4)	NE (2.6, NE)	0.7539 (0.1455, 2.5889)	0.4983	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Renal and urinary disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.5190
HER2 IHC 1+	214	14 (6.5)	200 (93.5)	NE (NE, NE)	100	5 (5.0)	95 (95.0)	NE (NE, NE)	0.8386 (0.2924, 2.4050) 0.7434	0.7443	
HER2 IHC 2+/ISH Negative	157	14 (8.9)	143 (91.1)	NE (NE, NE)	72	3 (4.2)	69 (95.8)	NE (NE, NE)	1.6350 (0.4650, 5.7489) 0.4435	0.4371	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Renal and urinary disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.1847
1	220	18 (8.2)	202 (91.8)	NE (NE, NE)	94	7 (7.4)	87 (92.6)	NE (NE, NE)	0.7930 (0.3263, 1.9273)	0.6100	
>=2	150	9 (6.0)	141 (94.0)	NE (NE, NE)	78	1 (1.3)	77 (98.7)	NE (NE, NE)	3.0089 (0.3725, 24.3052)	0.2778	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Renal and urinary disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.9488
Yes	233	19 (8.2)	214 (91.8)	NE (NE, NE)	112	6 (5.4)	106 (94.6)	NE (NE, NE)	1.1497 (0.4533, 2.9159) 0.7689	0.7673	
No	98	7 (7.1)	91 (92.9)	NE (NE, NE)	43	2 (4.7)	41 (95.3)	NE (NE, NE)	0.9344 (0.1862, 4.6884) 0.9343	0.9343	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Renal and urinary disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0565
<65	289	25 (8.7)	264 (91.3)	NE (NE, NE)	126	4 (3.2)	122 (96.8)	NE (NE, NE)	1.9526 (0.6707, 5.6845) 0.2197	0.2111	
>=65	82	3 (3.7)	79 (96.3)	NE (NE, NE)	46	4 (8.7)	42 (91.3)	NE (7.9, NE)	0.2945 (0.0643, 1.3491) 0.1154	0.0957	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Renal and urinary disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6155
<75	357	27 (7.6)	330 (92.4)	NE (NE, NE)	163	7 (4.3)	156 (95.7)	NE (NE, NE)	1.2495 (0.5364, 2.9108) 0.6056	0.6034	
>=75	14	1 (7.1)	13 (92.9)	NE (NE, NE)	9	1 (11.1)	8 (88.9)	NE (7.9, NE)	0.5345 (0.0329, 8.6917) 0.6598	0.6547	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Renal and urinary disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.3918
White	175	16 (9.1)	159 (90.9)	NE (NE, NE)	85	6 (7.1)	79 (92.9)	NE (NE, NE)	0.9895 (0.3817, 2.5656) 0.9827	0.9846	
Non-White	196	12 (6.1)	184 (93.9)	NE (NE, NE)	86	2 (2.3)	84 (97.7)	NE (NE, NE)	1.6258 (0.3552, 7.4428) 0.5312	0.5273	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Renal and urinary disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.5881
Asia	147	9 (6.1)	138 (93.9)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (7.9, NE)	2.3368 (0.2879, 18.9689) 0.4269	0.4134	
North America	58	10 (17.2)	48 (82.8)	NE (NE, NE)	28	4 (14.3)	24 (85.7)	NE (NE, NE)	0.9761 (0.3017, 3.1581) 0.9677	0.9747	
Europe + Israel	166	9 (5.4)	157 (94.6)	NE (NE, NE)	81	3 (3.7)	78 (96.3)	NE (NE, NE)	0.9618 (0.2538, 3.6446) 0.9543	0.9566	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Renal and urinary disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											
0	199	12 (6.0)	187 (94.0)	NE (NE, NE)	95	5 (5.3)	90 (94.7)	NE (NE, NE)	0.7737 (0.2672, 2.2403) 0.6363	0.6361	0.3086
1	172	16 (9.3)	156 (90.7)	NE (NE, NE)	77	3 (3.9)	74 (96.1)	NE (7.9, NE)	1.7672 (0.5056, 6.1768) 0.3725	0.3661	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Renal and urinary disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1116
0	60	5 (8.3)	55 (91.7)	NE (18.7, NE)	31	0	31 (100)	NE (NE, NE)	NE (NE, NE) 0.9960	0.2294	
1	107	9 (8.4)	98 (91.6)	NE (NE, NE)	48	3 (6.3)	45 (93.8)	NE (NE, NE)	0.9785 (0.2616, 3.6607) 0.9743	0.9767	
2	114	10 (8.8)	104 (91.2)	NE (NE, NE)	50	5 (10.0)	45 (90.0)	NE (NE, NE)	0.7363 (0.2507, 2.1622) 0.5775	0.5766	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Renal and urinary disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	4 (4.4)	86 (95.6) (NE, NE)	43	0	43 (100) (NE, NE)	NE (NE, NE) 0.9959	0.2181	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Renal and urinary disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.1592
PD	173	9 (5.2)	164 (94.8)	NE (NE, NE)	77	6 (7.8)	71 (92.2)	NE (NE, NE)	0.4337 (0.1485, 1.2665)	0.1160	
PR	48	2 (4.2)	46 (95.8)	NE (NE, NE)	21	1 (4.8)	20 (95.2)	NE (NE, NE)	0.1265 (0.0498, 6.4245)	0.6418	
SD	82	7 (8.5)	75 (91.5)	NE (NE, NE)	54	1 (1.9)	53 (98.1)	NE (7.9, NE)	3.3730 (0.4047, 28.1134)	0.2339	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Renal and urinary disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Reported history of CNS metastases											0.9049
Yes	37	4 (10.8)	33 (89.2)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	1.2302 (0.1364, 11.0914)	0.8532	
No	334	24 (7.2)	310 (92.8)	NE (NE, NE)	159	7 (4.4)	152 (95.6)	NE (NE, NE)	0.8535 (0.4651, 2.5966)	0.8284	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Renal and urinary disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.3772
Yes	24	2 (8.3)	22 (91.7)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9974	0.4736	
No	347	26 (7.5)	321 (92.5)	NE (NE, NE)	165	8 (4.8)	157 (95.2)	NE (NE, NE)	1.0662 (0.4748, 2.3946) 0.8765	0.8751	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Renal and urinary disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.8378
Normal Function	201	11 (5.5)	190 (94.5)	NE (NE, NE)	80	2 (2.5)	78 (97.5)	NE (NE, NE)	1.5475 (0.3352, 7.1446) 0.5759	0.5733	
Mild Impairment	123	11 (8.9)	112 (91.1)	NE (NE, NE)	65	3 (4.6)	62 (95.4)	NE (NE, NE)	1.2728 (0.3441, 4.7078) 0.7178	0.7166	
Moderate Impairment	41	5 (12.2)	36 (87.8)	NE (NE, NE)	23	3 (13.0)	20 (87.0)	NE (7.9, NE)	0.8115 (0.1932, 3.4082) 0.7754	0.7751	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Renal and urinary disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Hepatic function at baseline											
Normal Function	170	15 (8.8)	155 (91.2)	NE (NE, NE)	88	2 (2.3)	86 (97.7)	NE (NE, NE)	2.7142 (0.6155, 11.9689)	0.1692	0.0494
Mild Impairment	194	11 (5.7)	183 (94.3)	NE (NE, NE)	82	6 (7.3)	76 (92.7)	NE (7.9, NE)	0.4982 (0.1752, 1.4171)	0.1835	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Renal and urinary disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.0277
Yes	331	21 (6.3)	310 (93.7)	NE (NE, NE)	146	8 (5.5)	138 (94.5)	NE (NE, NE)	0.8525 (0.3731, 1.9478) 0.7050	0.7061	
No	40	7 (17.5)	33 (82.5)	NE (18.7, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9948	0.1000	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Renal and urinary disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.1417
Positive	329	24 (7.3)	305 (92.7)	NE (NE, NE)	152	8 (5.3)	144 (94.7)	NE (NE, NE)	0.9466 (0.4183, 2.1422) 0.8951	0.8966	
Negative	42	4 (9.5)	38 (90.5)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) 0.9957	0.1905	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Renal and urinary disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.3500
Positive	331	26 (7.9)	305 (92.1)	NE (NE, NE)	155	8 (5.2)	147 (94.8)	NE (NE, NE)	1.0742 (0.4792, 2.4082)	0.8620	0.8605
Negative	40	2 (5.0)	38 (95.0)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE)	0.9973	0.4397

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Hepatobiliary disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.2593
HER2 IHC 1+	214	12 (5.6)	202 (94.4)	NE (NE, NE)	100	5 (5.0)	95 (95.0)	NE (NE, NE)	0.6943 (0.2336, 2.0637) 0.5115	0.5085	
HER2 IHC 2+/ISH Negative	157	13 (8.3)	144 (91.7)	NE (NE, NE)	72	2 (2.8)	70 (97.2)	NE (NE, NE)	1.8624 (0.4115, 8.4284) 0.4195	0.4100	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Hepatobiliary disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.1401
1	220	15 (6.8)	205 (93.2)	NE (NE, NE)	94	6 (6.4)	88 (93.6)	NE (NE, NE)	0.7617 (0.2887, 2.0097) 0.5824	0.5804	
>=2	150	10 (6.7)	140 (93.3)	NE (NE, NE)	78	1 (1.3)	77 (98.7)	NE (NE, NE)	2.5624 (0.3183, 20.6264) 0.3766	0.3595	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Hepatobiliary disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.9456
Yes	233	18 (7.7)	215 (92.3)	NE (NE, NE)	112	4 (3.6)	108 (96.4)	NE (NE, NE)	1.4672 (0.4859, 4.4301) 0.4965	0.4939	
No	98	5 (5.1)	93 (94.9)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	1.0704 (0.1199, 9.5559) 0.9515	0.9515	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Hepatobiliary disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6904
<65	289	18 (6.2)	271 (93.8)	NE (NE, NE)	126	5 (4.0)	121 (96.0)	NE (NE, NE)	1.0268 (0.3716, 2.8370) 0.9593	0.9588	
>=65	82	7 (8.5)	75 (91.5)	NE (NE, NE)	46	2 (4.3)	44 (95.7)	NE (NE, NE)	1.1982 (0.2414, 5.9476) 0.8250	0.8247	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Hepatobiliary disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7380
<75	357	22 (6.2)	335 (93.8)	NE (NE, NE)	163	6 (3.7)	157 (96.3)	NE (NE, NE)	1.0180 (0.4025, 2.5747) 0.9699	0.9697	
>=75	14	3 (21.4)	11 (78.6)	NE (8.5, NE)	9	1 (11.1)	8 (88.9)	NE (1.2, NE)	1.6998 (0.1738, 16.6225) 0.6484	0.6447	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Hepatobiliary disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.8445
White	175	13 (7.4)	162 (92.6)	NE (NE, NE)	85	4 (4.7)	81 (95.3)	NE (NE, NE)	1.0626 (0.3374, 3.3458) 0.9174	0.9160	
Non-White	196	12 (6.1)	184 (93.9)	NE (NE, NE)	86	3 (3.5)	83 (96.5)	NE (NE, NE)	1.0573 (0.2896, 3.8596) 0.9328	0.9330	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Hepatobiliary disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.4074
Asia	147	8 (5.4)	139 (94.6)	NE (NE, NE)	63	3 (4.8)	60 (95.2)	NE (NE, NE)	0.7305 (0.1876, 2.8440) 0.6507	0.6489	
North America	58	3 (5.2)	55 (94.8)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9966	0.3028	
Europe + Israel	166	14 (8.4)	152 (91.6)	NE (NE, NE)	81	4 (4.9)	77 (95.1)	NE (NE, NE)	1.0706 (0.3411, 3.3602) 0.9070	0.9062	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Hepatobiliary disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
ECOG PS											
0	199	13 (6.5)	186 (93.5)	NE (NE, NE)	95	5 (5.3)	90 (94.7)	NE (NE, NE)	0.8751 (0.3048, 2.5128) 0.8042	0.8037	0.3504
1	172	12 (7.0)	160 (93.0)	NE (NE, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	1.4108 (0.3030, 6.5681) 0.6610	0.6597	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Hepatobiliary disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1319
0	60	3 (5.0)	57 (95.0)	NE (NE, NE)	31	3 (9.7)	28 (90.3)	NE (NE, NE)	0.4131 (0.0817, 2.0899)	0.2702	
1	107	8 (7.5)	99 (92.5)	NE (NE, NE)	48	3 (6.3)	45 (93.8)	NE (NE, NE)	0.7878 (0.2045, 3.0347)	0.7284	
2	114	8 (7.0)	106 (93.0)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	0.7289 (NE, NE)	0.1266	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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SOC: Hepatobiliary disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 (6.7)	84 (93.3)	NE (NE, NE)	43 (2.3)	42 (97.7)	NE (NE, NE)	1.5495 (0.1789, 13.4191) 0.6909	0.6888	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Hepatobiliary disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.1409
PD	173	13 (7.5)	160 (92.5)	NE (NE, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	1.9091 (0.4223, 8.6295)	0.3926	
PR	48	0	48 (100)	NE (NE, NE)	21	1 (4.8)	20 (95.2)	NE (NE, NE)	0.4008 (0.0000, )	0.1306	
SD	82	8 (9.8)	74 (90.2)	NE (NE, NE)	54	3 (5.6)	51 (94.4)	NE (NE, NE)	1.1520 (0.2948, 4.5020)	0.8391	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Hepatobiliary disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.5430
Yes	37	1 (2.7)	36 (97.3)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9984	0.6726	
No	334	24 (7.2)	310 (92.8)	NE (NE, NE)	159	7 (4.4)	152 (95.6)	NE (NE, NE)	1.0347 (0.4359, 2.4563) 0.9383	0.9380	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Hepatobiliary disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											1.0000
Yes	24	0	24 (100)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE)		
No	347	25 (7.2)	322 (92.8)	NE (NE, NE)	165	7 (4.2)	158 (95.8)	NE (NE, NE)	1.0672 (0.4516, 2.5223) 0.8821	0.8821	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Hepatobiliary disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.6610
Normal Function	201	10 (5.0)	191 (95.0)	NE (NE, NE)	80	2 (2.5)	78 (97.5)	NE (NE, NE)	1.4457 (0.3097, 6.7494) 0.6392	0.6367	
Mild Impairment	123	10 (8.1)	113 (91.9)	NE (NE, NE)	65	4 (6.2)	61 (93.8)	NE (NE, NE)	0.6756 (0.2000, 2.2818) 0.5277	0.5258	
Moderate Impairment	41	5 (12.2)	36 (87.8)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	2.1943 (0.2541, 18.9498) 0.4750	0.4638	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Hepatobiliary disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.0801
Normal Function	170	10 (5.9)	160 (94.1)	NE (NE, NE)	88	1 (1.1)	87 (98.9)	NE (NE, NE)	3.6170 (0.4543, 28.7992) 0.2245	0.1946	
Mild Impairment	194	13 (6.7)	181 (93.3)	NE (NE, NE)	82	6 (7.3)	76 (92.7)	NE (NE, NE)	0.4504 (0.1620, 1.2523) 0.1263	0.1181	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Hepatobiliary disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.3881
Yes	331	24 (7.3)	307 (92.7)	NE (NE, NE)	146	6 (4.1)	140 (95.9)	NE (NE, NE)	1.1261 (0.4518, 2.8065) 0.7988	0.7991	
No	40	1 (2.5)	39 (97.5)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	0.6477 (0.0405, 10.3590) 0.7588	0.7570	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Hepatobiliary disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.1881
Positive	329	23 (7.0)	306 (93.0)	NE (NE, NE)	152	5 (3.3)	147 (96.7)	NE (NE, NE)	1.3426 (0.5005, 3.6016) 0.5585	0.5571	
Negative	42	2 (4.8)	40 (95.2)	NE (NE, NE)	20	2 (10.0)	18 (90.0)	NE (NE, NE)	0.2371 (0.0215, 2.6159) 0.2400	0.2000	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Hepatobiliary disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.1481
Positive	331	23 (6.9)	308 (93.1)	NE (NE, NE)	155	5 (3.2)	150 (96.8)	NE (NE, NE)	1.3606 (0.5070, 3.6512) 0.5410	0.5394	
Negative	40	2 (5.0)	38 (95.0)	NE (NE, NE)	17	2 (11.8)	15 (88.2)	NE (NE, NE)	0.2020 (0.0183, 2.2334) 0.1920	0.1471	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Ear and labyrinth disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.2849
HER2 IHC 1+	214	16 (7.5)	198 (92.5)	NE (23.7, NE)	100	2 (2.0)	98 (98.0)	NE (NE, NE)	1.9284 (0.4294, 8.6593) 0.3915	0.3835	
HER2 IHC 2+/ISH Negative	157	5 (3.2)	152 (96.8)	NE (NE, NE)	72	2 (2.8)	70 (97.2)	NE (NE, NE)	0.8141 (0.1558, 4.2529) 0.8074	0.8071	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Ear and labyrinth disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.4207
1	220	12 (5.5)	208 (94.5)	NE (23.7, NE)	94	3 (3.2)	91 (96.8)	NE (NE, NE)	0.9230 (0.2503, 3.4037) 0.9042	0.9042	
>=2	150	9 (6.0)	141 (94.0)	NE (NE, NE)	78	1 (1.3)	77 (98.7)	NE (NE, NE)	2.8479 (0.3532, 22.9627) 0.3257	0.3047	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.5642
Yes	233	12 (5.2)	221 (94.8)	NE (NE, NE)	112	3 (2.7)	109 (97.3)	NE (NE, NE)	1.0125 (0.2730, 3.7552) 0.9851	0.9851	
No	98	8 (8.2)	90 (91.8)	NE (23.7, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	2.2597 (0.2752, 18.5531) 0.4479	0.4356	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2406
<65	289	18 (6.2)	271 (93.8)	NE (NE, NE)	126	2 (1.6)	124 (98.4)	NE (NE, NE)	2.0451 (0.4645, 9.0046) 0.3442	0.3344	
>=65	82	3 (3.7)	79 (96.3)	23.7 (23.7, NE)	46	2 (4.3)	44 (95.7)	NE (NE, NE)	0.5361 (0.0755, 3.8073) 0.5331	0.5265	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9999
<75	357	21 (5.9)	336 (94.1)	NE (NE, NE)	163	4 (2.5)	159 (97.5)	NE (NE, NE)	1.3094 (0.4376, 3.9179) 0.6298	0.6287	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Ear and labyrinth disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.7129
White	175	12 (6.9)	163 (93.1)	NE (NE, NE)	85	2 (2.4)	83 (97.6)	NE (NE, NE)	1.7221 (0.3772, 7.8631) 0.4830	0.4779	
Non-White	196	9 (4.6)	187 (95.4)	NE (23.7, NE)	86	2 (2.3)	84 (97.7)	NE (NE, NE)	1.0651 (0.2183, 5.1969) 0.9378	0.9378	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Ear and labyrinth disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.3376
Asia	147	7 (4.8)	140 (95.2)	NE (23.7, NE)	63	2 (3.2)	61 (96.8)	NE (NE, NE)	0.7630 (0.1482, 3.9270) 0.7462	0.7456	
North America	58	2 (3.4)	56 (96.6)	NE (NE, NE)	28	1 (3.6)	27 (96.4)	NE (NE, NE)	0.1927 (0.0090, 4.1479) 0.2930	0.2594	
Europe + Israel	166	12 (7.2)	154 (92.8)	NE (NE, NE)	81	1 (1.2)	80 (98.8)	NE (NE, NE)	3.9302 (0.5054, 30.5636) 0.1909	0.1586	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Ear and labyrinth disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.4686
0	199	12 (6.0)	187 (94.0)	NE (23.7, NE)	95	3 (3.2)	92 (96.8)	NE (NE, NE)	0.9895 (0.2700, 3.6263) 0.9872	0.9873	
1	172	9 (5.2)	163 (94.8)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	2.5863 (0.3195, 20.9328) 0.3731	0.3559	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Ear and labyrinth disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.4178
0	60	2 (3.3)	58 (96.7)	NE (NE, NE)	31	1 (3.2)	30 (96.8)	NE (NE, NE)	0.6816 (0.0600, 7.7370) 0.7571	0.7558	
1	107	6 (5.6)	101 (94.4)	NE (NE, NE)	48	1 (2.1)	47 (97.9)	NE (NE, NE)	2.1773 (0.2606, 18.1885) 0.4725	0.4614	
2	114	6 (5.3)	108 (94.7)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	NE (NE, NE) 0.9952	0.3960	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Ear and labyrinth disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 (7.8)	83 (92.2)	NE (23.7, NE)	43 (4.7)	41 (95.3)	NE (NE, NE)	0.9010 (0.1745, 4.6531) 0.9009	0.9009	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Ear and labyrinth disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.8578
PD	173	6 (3.5)	167 (96.5)	NE (NE, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	1.0288 (0.2056, 5.1486) 0.9725	0.9723	
PR	48	2 (4.2)	46 (95.8)	NE (NE, NE)	21	1 (4.8)	20 (95.2)	NE (NE, NE)	0.4252 (0.0352, 5.1279) 0.5008	0.4897	
SD	82	3 (3.7)	79 (96.3)	23.7 (23.7, NE)	54	1 (1.9)	53 (98.1)	NE (NE, NE)	0.7709 (0.0656, 9.0543) 0.8360	0.8356	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Ear and labyrinth disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.3484
Yes	37	3 (8.1)	34 (91.9)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9965	0.3223	
No	334	18 (5.4)	316 (94.6)	NE (23.7, NE)	159	4 (2.5)	155 (97.5)	NE (NE, NE)	1.1130 (0.3656, 3.3883) 0.8505	0.8505	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Ear and labyrinth disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.4345
Yes	24	2 (8.3)	22 (91.7)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9971	0.4137	
No	347	19 (5.5)	328 (94.5)	NE (23.7, NE)	165	4 (2.4)	161 (97.6)	NE (NE, NE)	1.1920 (0.3942, 3.6038) 0.7557	0.7554	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Ear and labyrinth disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.5368
Normal Function	201	11 (5.5)	190 (94.5)	NE (23.7, NE)	80	2 (2.5)	78 (97.5)	NE (NE, NE)	1.1812 (0.2507, 5.5653) 0.8332	0.8330	
Mild Impairment	123	8 (6.5)	115 (93.5)	NE (NE, NE)	65	2 (3.1)	63 (96.9)	NE (NE, NE)	1.1309 (0.2281, 5.6080) 0.8803	0.8802	
Moderate Impairment	41	2 (4.9)	39 (95.1)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9969	0.3500	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Ear and labyrinth disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.7802
Normal Function	170	11 (6.5)	159 (93.5)	NE (23.7, NE)	88	2 (2.3)	86 (97.7)	NE (NE, NE)	1.4016 (0.2992, 6.5660) 0.6683	0.6667	
Mild Impairment	194	10 (5.2)	184 (94.8)	NE (NE, NE)	82	2 (2.4)	80 (97.6)	NE (NE, NE)	1.3604 (0.2906, 6.3690) 0.6960	0.6947	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Ear and labyrinth disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.5514
Yes	331	20 (6.0)	311 (94.0)	NE (23.7, NE)	146	4 (2.7)	142 (97.3)	NE (NE, NE)	1.3386 (0.4486, 3.9941) 0.6011	0.5997	
No	40	1 (2.5)	39 (97.5)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9985	0.8137	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Ear and labyrinth disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.5570
Positive	329	20 (6.1)	309 (93.9)	NE (23.7, NE)	152	4 (2.6)	148 (97.4)	NE (NE, NE)	1.3272 (0.4434, 3.9729) 0.6129	0.6116	
Negative	42	1 (2.4)	41 (97.6)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) 0.9984	0.6780	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Ear and labyrinth disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.5939
Positive	331	20 (6.0)	311 (94.0)	NE (23.7, NE)	155	4 (2.6)	151 (97.4)	NE (NE, NE)	1.3480 (0.4501, 4.0366)	0.5936	0.5922
Negative	40	1 (2.5)	39 (97.5)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) 0.9980		0.7518

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Reproductive system and breast disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.5254
HER2 IHC 1+	214	12 (5.6)	202 (94.4)	NE (NE, NE)	100	3 (3.0)	97 (97.0)	NE (NE, NE)	1.0511 (0.2839, 3.8924) 0.9405	0.9413	
HER2 IHC 2+/ISH Negative	157	8 (5.1)	149 (94.9)	NE (NE, NE)	72	1 (1.4)	71 (98.6)	NE (NE, NE)	2.6715 (0.3293, 21.6733) 0.3576	0.3388	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Reproductive system and breast disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.1504
1	220	13 (5.9)	207 (94.1)	NE (NE, NE)	94	1 (1.1)	93 (98.9)	NE (NE, NE)	3.7565 (0.4857, 29.0500) 0.2048	0.1736	
>=2	150	7 (4.7)	143 (95.3)	NE (NE, NE)	78	3 (3.8)	75 (96.2)	NE (NE, NE)	0.7249 (0.1771, 2.9665) 0.6545	0.6535	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Reproductive system and breast disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.9309
Yes	233	11 (4.7)	222 (95.3)	NE (NE, NE)	112	2 (1.8)	110 (98.2)	NE (NE, NE)	1.4536 (0.3132, 6.7466) 0.6329	0.6310	
No	98	5 (5.1)	93 (94.9)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	1.7840 (0.2071, 15.3655) 0.5983	0.5919	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Reproductive system and breast disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3019
<65	289	18 (6.2)	271 (93.8)	NE (NE, NE)	126	4 (3.2)	122 (96.8)	NE (NE, NE)	1.1443 (0.3782, 3.4623) 0.8113	0.8116	
>=65	82	2 (2.4)	80 (97.6)	NE (NE, NE)	46	0	46 (100)	NE (NE, NE)	NE (NE, NE) 0.9967	0.2932	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Reproductive system and breast disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9999
<75	357	20 (5.6)	337 (94.4)	NE (NE, NE)	163	4 (2.5)	159 (97.5)	NE (NE, NE)	1.4177 (0.4745, 4.2359) 0.5320	0.5298	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Reproductive system and breast disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.6618
White	175	12 (6.9)	163 (93.1)	NE (NE, NE)	85	2 (2.4)	83 (97.6)	NE (NE, NE)	2.1360 (0.4720, 9.6657) 0.3245	0.3130	
Non-White	196	8 (4.1)	188 (95.9)	NE (NE, NE)	86	2 (2.3)	84 (97.7)	NE (NE, NE)	0.8596 (0.1714, 4.3099) 0.8541	0.8539	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.7453
Asia	147	7 (4.8)	140 (95.2)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (NE, NE)	1.5367 (0.1804, 13.0910) 0.6942	0.6921	
North America	58	6 (10.3)	52 (89.7)	NE (15.8, NE)	28	2 (7.1)	26 (92.9)	NE (NE, NE)	0.8099 (0.1512, 4.3386) 0.8055	0.8052	
Europe + Israel	166	7 (4.2)	159 (95.8)	NE (NE, NE)	81	1 (1.2)	80 (98.8)	NE (NE, NE)	2.7733 (0.3380, 22.7538) 0.3422	0.3219	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.8.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Reproductive system and breast disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.9228
0	199	10 (5.0)	189 (95.0)	NE (NE, NE)	95	2 (2.1)	93 (97.9)	NE (NE, NE)	1.3498 (0.2890, 6.3034) 0.7029	0.7021	
1	172	10 (5.8)	162 (94.2)	NE (19.3, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	1.6205 (0.3462, 7.5845) 0.5399	0.5359	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Reproductive system and breast disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.3993
0	60	2 (3.3)	58 (96.7)	NE (NE, NE)	31	2 (6.5)	29 (93.5)	NE (NE, NE)	0.4436 (0.0622, 3.1655) 0.4176	0.4049	
1	107	7 (6.5)	100 (93.5)	NE (NE, NE)	48	1 (2.1)	47 (97.9)	NE (NE, NE)	2.2798 (0.2761, 18.8221) 0.4442	0.4315	
2	114	9 (7.9)	105 (92.1)	NE (19.3, NE)	50	1 (2.0)	49 (98.0)	NE (NE, NE)	2.3753 (0.2880, 19.5881) 0.4216	0.4078	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Reproductive system and breast disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	2 (2.2)	88 (97.8)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9977	0.5185	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Reproductive system and breast disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.1464
PD	173	7 (4.0)	166 (96.0)	NE (NE, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	1.2718 (0.2627, 6.1577)	0.7651	
PR	48	6 (12.5)	42 (87.5)	19.3 (15.8, NE)	21	0	21 (100)	NE (NE, NE)	NE (NE, NE)	0.3879	
SD	82	5 (6.1)	77 (93.9)	NE (NE, NE)	54	0	54 (100)	NE (NE, NE)	NE (NE, NE)	0.1560	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Reproductive system and breast disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.9999
Yes	37	0	37 (100)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE)		
No	334	20 (6.0)	314 (94.0)	NE (NE, NE)	159	4 (2.5)	155 (97.5)	NE (NE, NE)	1.5117 (0.5064, 4.5132) 0.4590	0.4555	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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SOC: Reproductive system and breast disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.9999
Yes	24	0	24 (100)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE)		
No	347	20 (5.8)	327 (94.2)	NE (NE, NE)	165	4 (2.4)	161 (97.6)	NE (NE, NE)	1.4857 (0.4974, 4.4379) 0.4782	0.4751	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.1599
Normal Function	201	14 (7.0)	187 (93.0)	NE (NE, NE)	80	1 (1.3)	79 (98.8)	NE (NE, NE)	2.9953 (0.3866, 23.2091) 0.2937	0.2699	
Mild Impairment	123	4 (3.3)	119 (96.7)	NE (NE, NE)	65	3 (4.6)	62 (95.4)	NE (NE, NE)	0.6316 (0.1410, 2.8298) 0.5481	0.5447	
Moderate Impairment	41	1 (2.4)	40 (97.6)	NE (19.3, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.6029
Normal Function	170	11 (6.5)	159 (93.5)	NE (NE, NE)	88	3 (3.4)	85 (96.6)	NE (NE, NE)	1.0713 (0.2853, 4.0232) 0.9187	0.9190	
Mild Impairment	194	9 (4.6)	185 (95.4)	NE (NE, NE)	82	1 (1.2)	81 (98.8)	NE (NE, NE)	2.6687 (0.3348, 21.2739) 0.3540	0.3351	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.5086
Yes	331	14 (4.2)	317 (95.8)	NE (NE, NE)	146	2 (1.4)	144 (98.6)	NE (NE, NE)	1.9586 (0.4371, 8.7766) 0.3797	0.3713	
No	40	6 (15.0)	34 (85.0)	NE (19.3, NE)	26	2 (7.7)	24 (92.3)	NE (NE, NE)	1.1993 (0.2309, 6.2293) 0.8288	0.8319	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.9573
Positive	329	15 (4.6)	314 (95.4)	NE (NE, NE)	152	3 (2.0)	149 (98.0)	NE (NE, NE)	1.4268 (0.4054, 5.0219)	0.5776	
Negative	42	5 (11.9)	37 (88.1)	19.3 (19.3, NE)	20	1 (5.0)	19 (95.0)	NE (NE, NE)	1.8007 (0.2011, 16.1247)	0.5937	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.8.2 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Reproductive system and breast disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.7576
Positive	331	16 (4.8)	315 (95.2)	NE (NE, NE)	155	3 (1.9)	152 (98.1)	NE (NE, NE)	1.4786 (0.4200, 5.2061)	0.5396	
Negative	40	4 (10.0)	36 (90.0)	NE (NE, NE)	17	1 (5.9)	16 (94.1)	NE (2.9, NE)	1.3431 (0.1479, 12.1993)	0.7925	

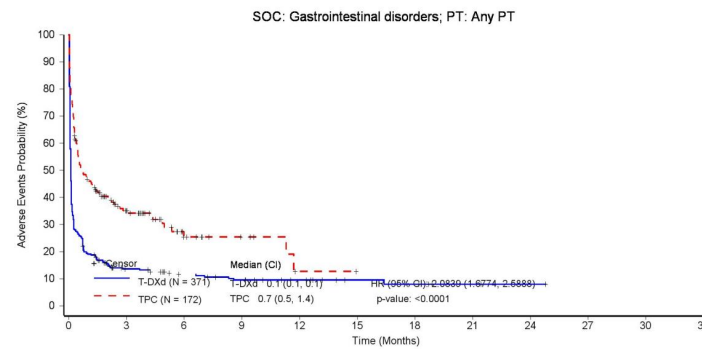
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	37	24	18	12	6	5	2	1	0	0	0
TPC (N = 172)	172	41	12	6	1	0	0	0	0	0	0	0

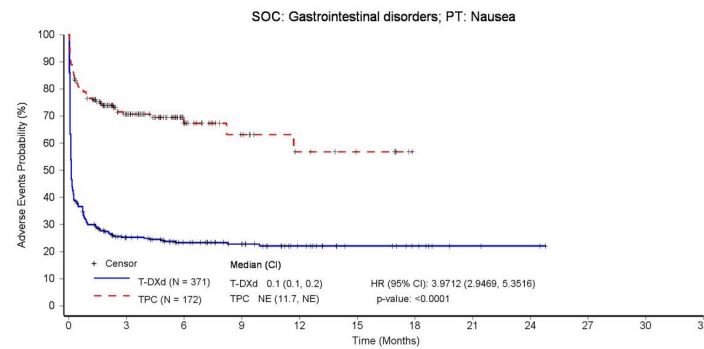
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	73	52	37	22	13	8	3	2	0	0	0
TPC (N = 172)	172	80	30	14	8	5	0	0	0	0	0	0

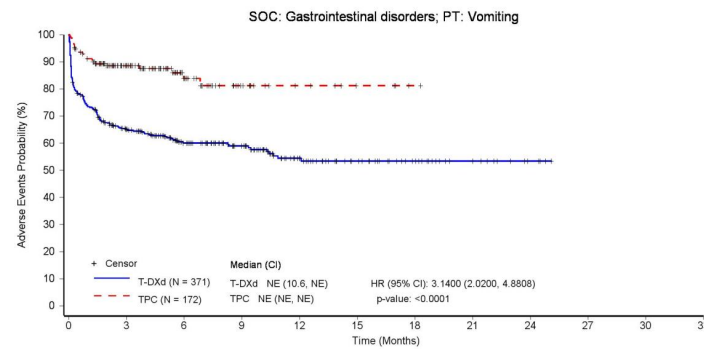
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	205	142	99	54	36	23	11	4	0	0	0
TPC (N = 172)	172	97	39	16	8	4	1	0	0	0	0	0

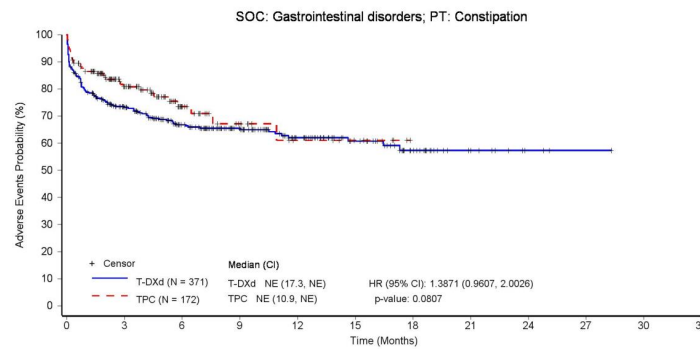
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

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 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	225	159	116	74	46	25	9	3	1	0	0
TPC (N = 172)	172	85	31	15	8	5	0	0	0	0	0	0

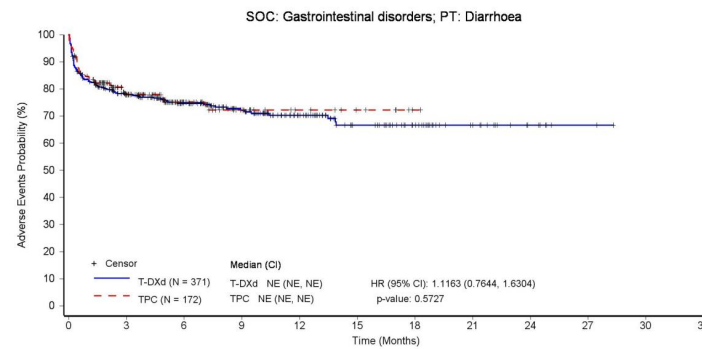
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	240	175	128	79	49	32	16	7	2	0	0
TPC (N = 172)	172	82	34	18	10	6	1	0	0	0	0	0

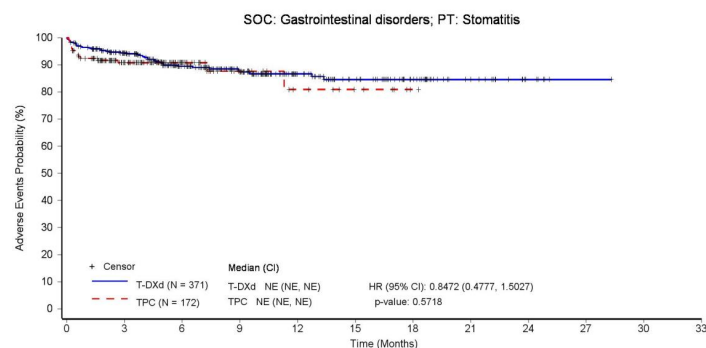
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	295	210	150	90	63	38	17	6	1	0	0
TPC (N = 172)	172	100	43	20	10	6	1	0	0	0	0	0

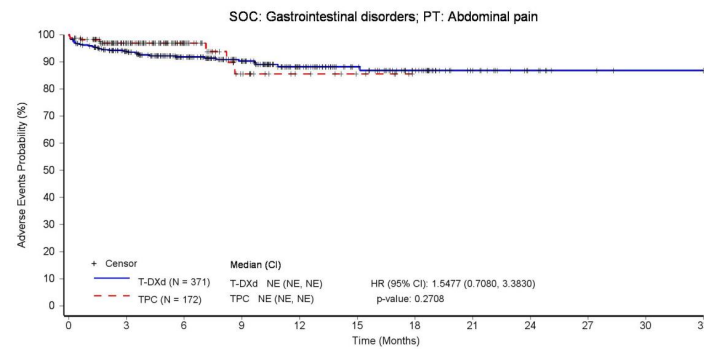
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	292	215	156	94	63	41	18	8	3	1	0
TPC (N = 172)	172	106	43	18	9	5	0	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

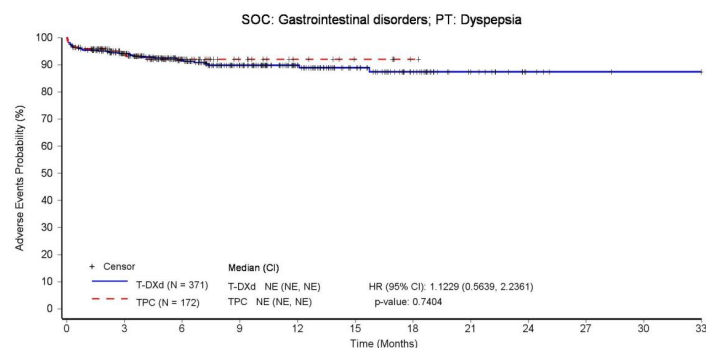
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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	295	216	153	100	64	36	15	5	2	1	0
TPC (N = 172)	172	100	37	16	9	5	1	0	0	0	0	0

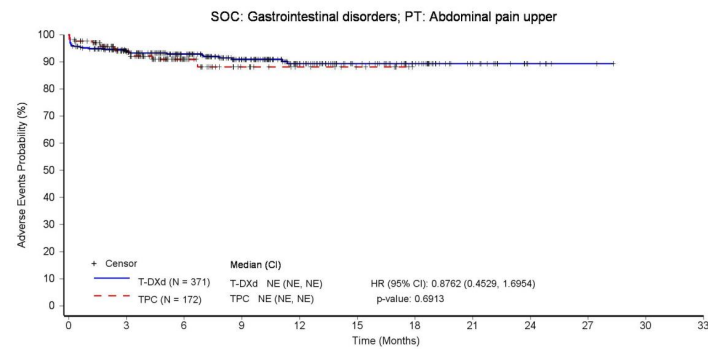
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	294	221	157	98	64	41	18	6	2	0	0
TPC (N = 172)	172	102	41	17	10	6	0	0	0	0	0	0

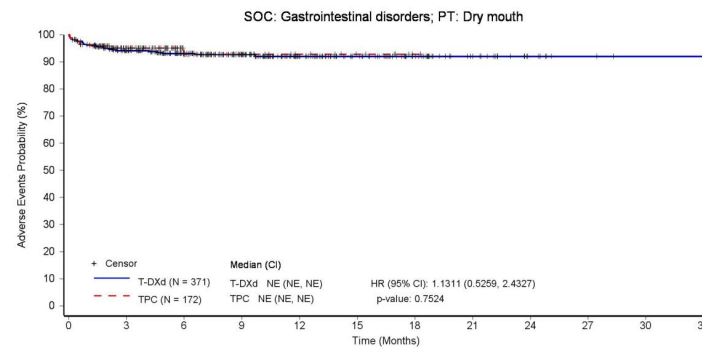
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	295	225	167	104	69	42	20	8	3	1	0
TPC (N = 172)	172	100	40	17	10	6	1	0	0	0	0	0

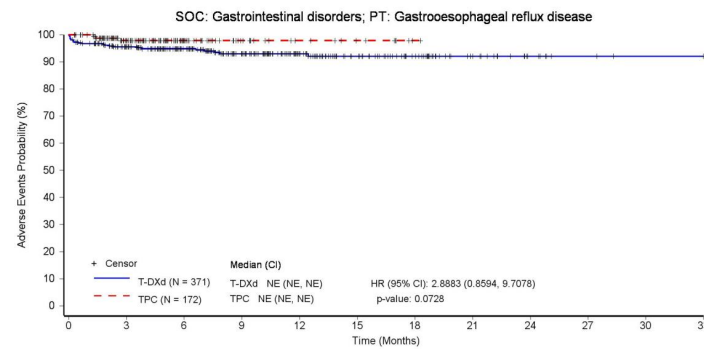
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	299	226	163	102	67	42	19	8	3	1	0
TPC (N = 172)	172	105	44	20	11	7	1	0	0	0	0	0

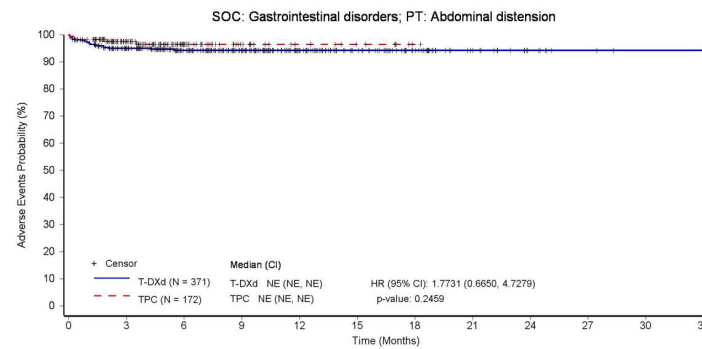
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	297	223	164	104	69	41	18	8	3	1	0
TPC (N = 172)	172	104	44	20	11	7	1	0	0	0	0	0

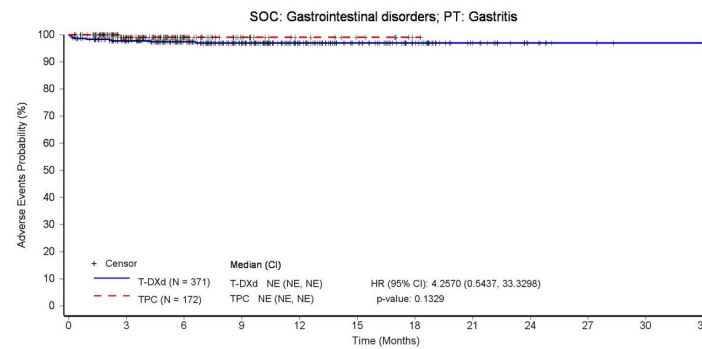
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	307	233	171	109	73	44	20	8	3	1	0
TPC (N = 172)	172	106	44	20	11	7	1	0	0	0	0	0

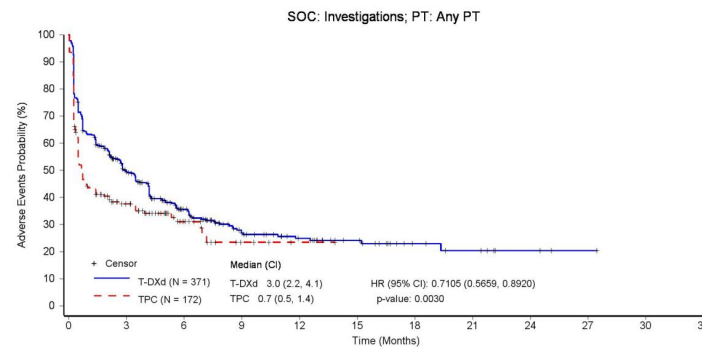
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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	161	90	49	33	21	10	7	3	1	0	0
TPC (N = 172)	172	46	17	4	1	0	0	0	0	0	0	0

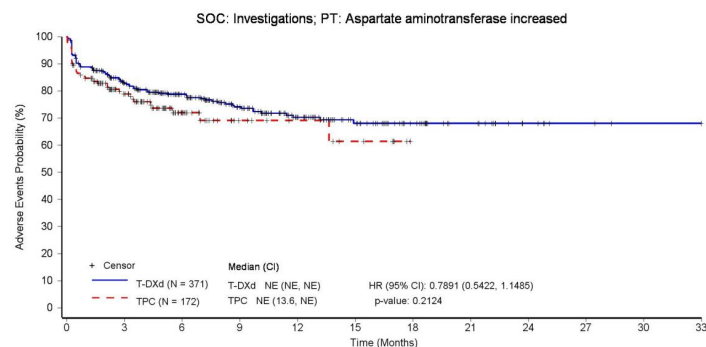
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	265	193	137	88	54	30	17	7	3	1	0
TPC (N = 172)	172	90	34	13	9	6	0	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

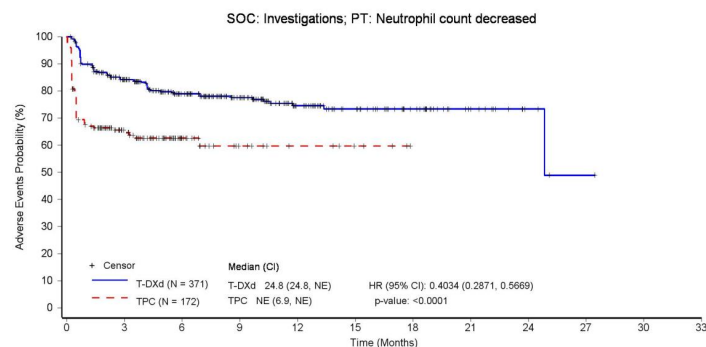
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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	266	188	135	79	54	32	13	4	1	0	0
TPC (N = 172)	172	71	27	12	7	4	0	0	0	0	0	0

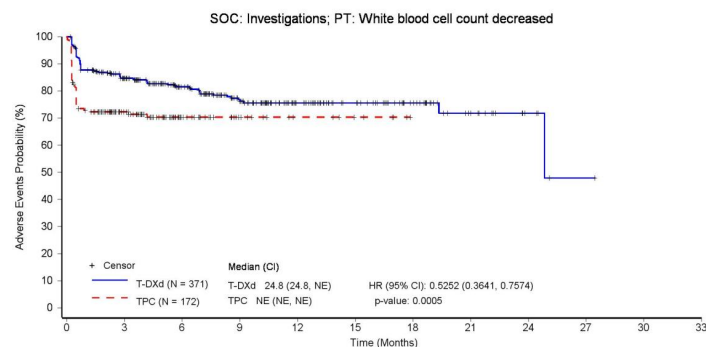
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	266	194	135	84	57	34	14	5	1	0	0
TPC (N = 172)	172	80	33	15	8	5	0	0	0	0	0	0

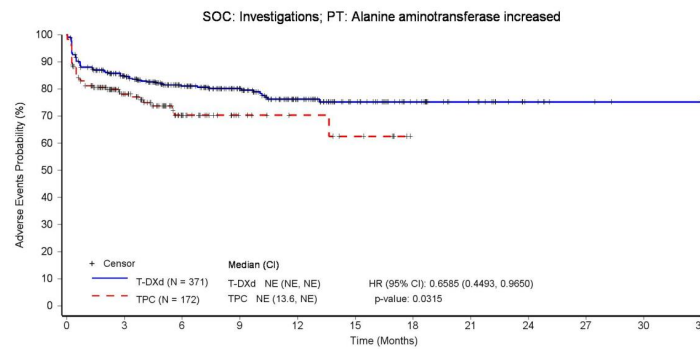
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	267	194	142	87	53	30	18	7	3	1	0
TPC (N = 172)	172	86	33	13	9	6	0	0	0	0	0	0

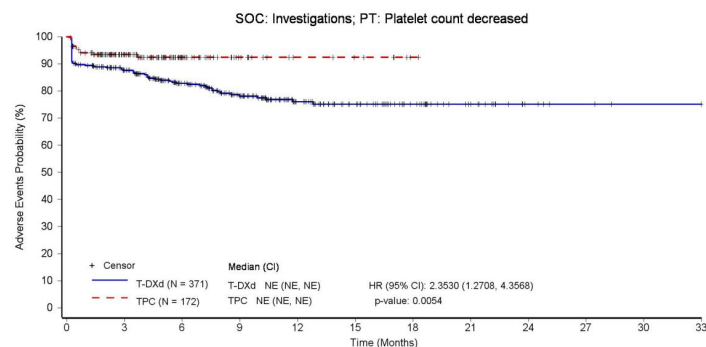
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	277	201	145	90	61	35	17	6	3	1	0
TPC (N = 172)	172	102	41	17	8	6	1	0	0	0	0	0

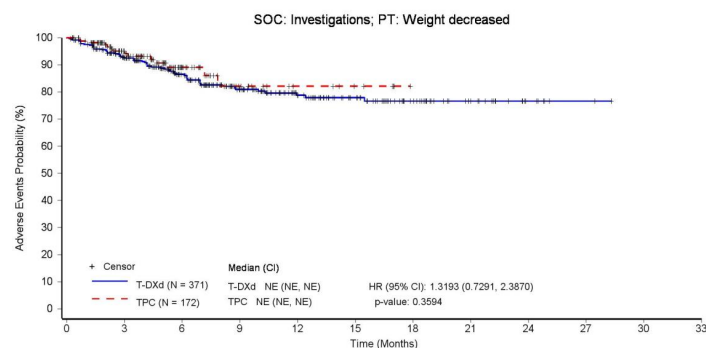
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	291	208	141	94	64	38	19	7	2	0	0
TPC (N = 172)	172	103	41	16	8	5	0	0	0	0	0	0

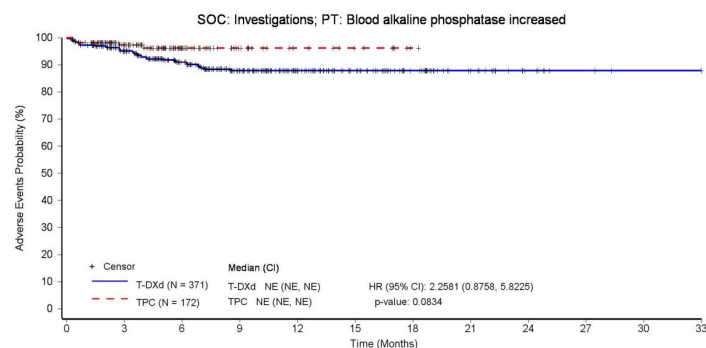
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	300	219	156	100	66	38	19	8	3	1	0
TPC (N = 172)	172	105	44	20	11	7	1	0	0	0	0	0

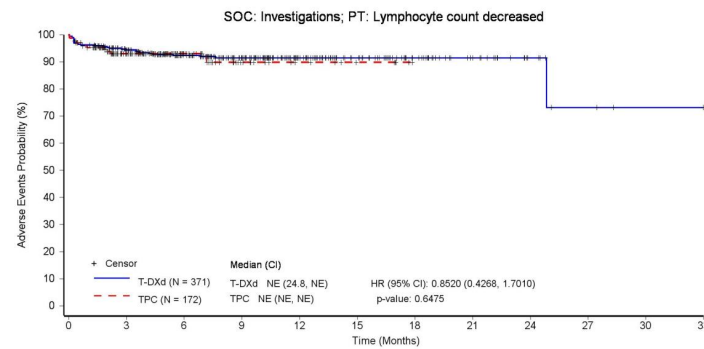
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	298	222	165	104	68	39	20	8	3	1	0
TPC (N = 172)	172	100	40	17	9	5	0	0	0	0	0	0

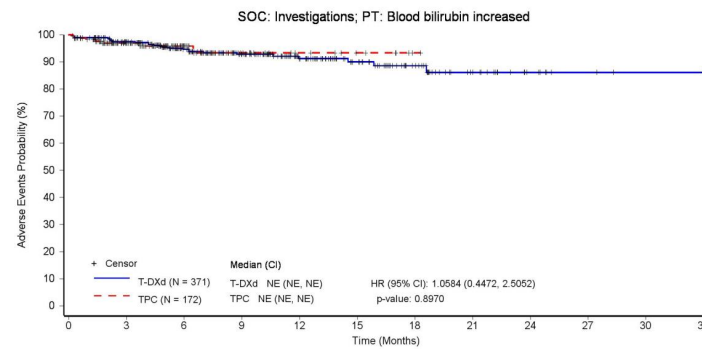
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	309	230	166	106	70	42	19	8	3	1	0
TPC (N = 172)	172	106	44	19	10	6	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

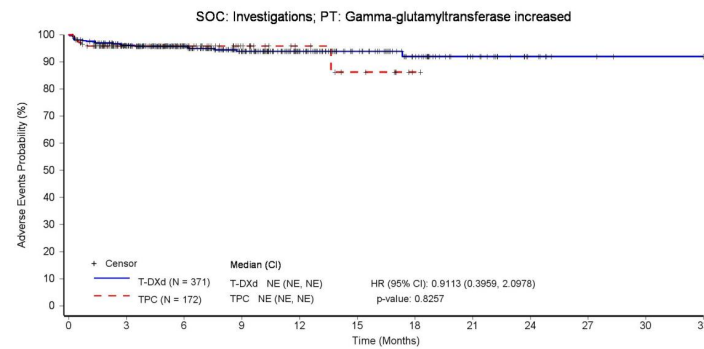
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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	304	233	168	107	70	42	20	8	3	1	0
TPC (N = 172)	172	101	42	20	11	7	1	0	0	0	0	0

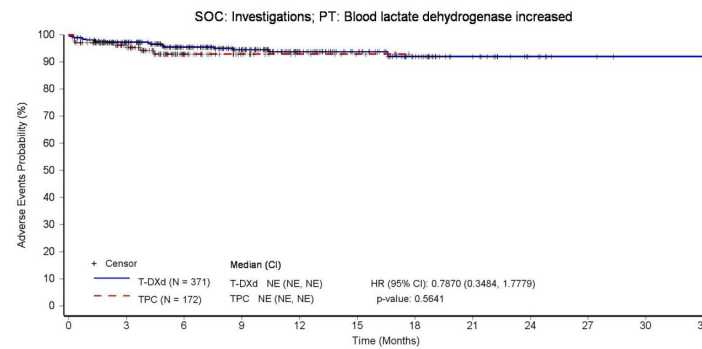
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	308	227	165	103	69	40	19	8	3	1	0
TPC (N = 172)	172	103	39	18	9	5	0	0	0	0	0	0

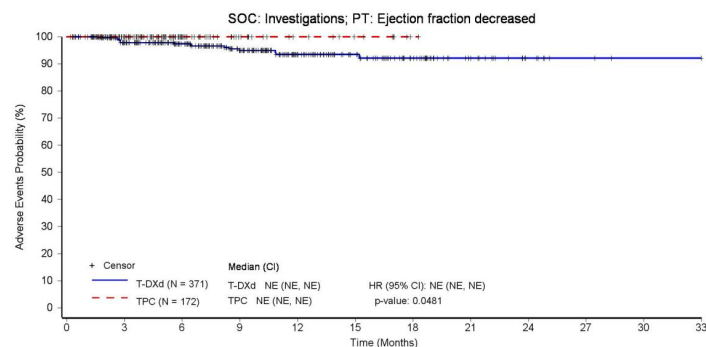
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	308	234	170	106	70	42	19	8	3	1	0
TPC (N = 172)	172	107	44	20	11	7	1	0	0	0	0	0

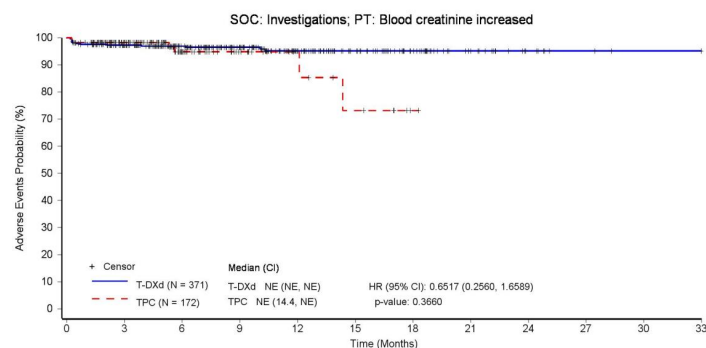
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	307	231	169	108	71	42	19	8	3	1	0
TPC (N = 172)	172	106	42	19	10	6	1	0	0	0	0	0

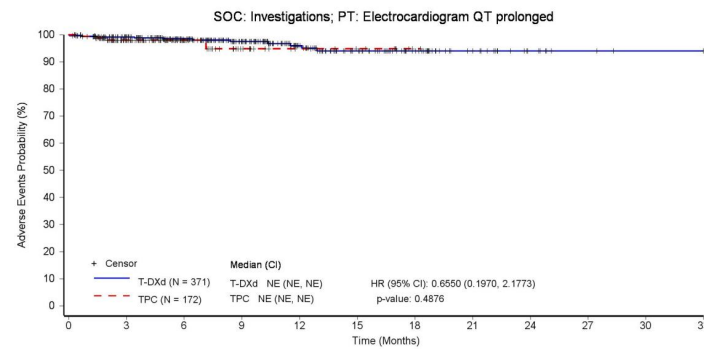
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rtf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	312	235	170	106	69	41	19	8	3	1	0
TPC (N = 172)	172	104	42	19	10	7	1	0	0	0	0	0

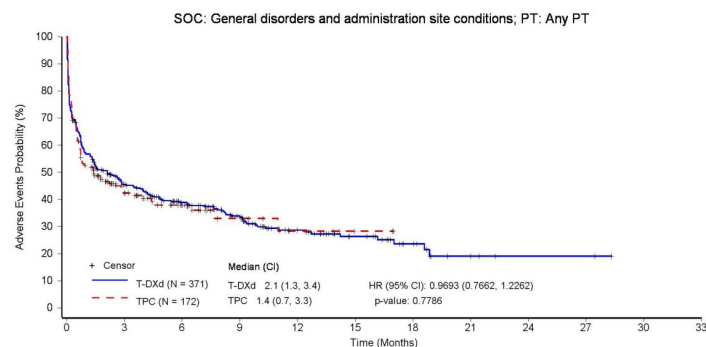
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	145	104	74	42	25	13	4	2	2	0	0
TPC (N = 172)	172	48	22	10	5	2	0	0	0	0	0	0

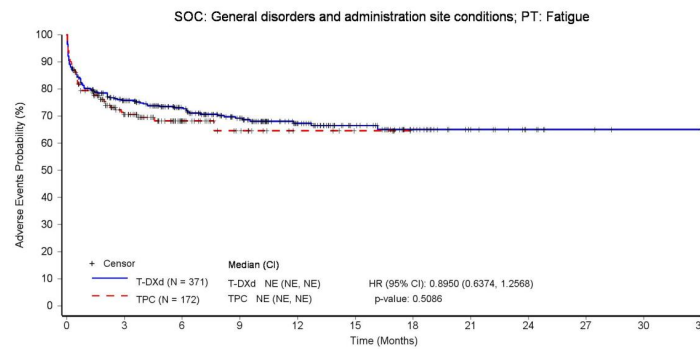
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

T-DXd (N = 371)	371	239	184	133	85	54	30	14	7	3	1	0
TPC (N = 172)	172	79	33	15	7	4	0	0	0	0	0	0

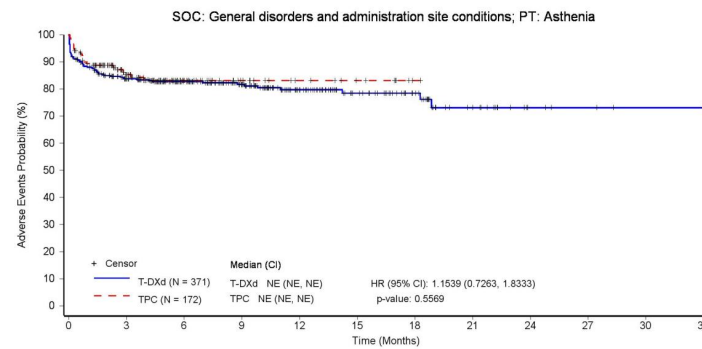
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	261	196	146	90	57	36	16	5	3	1	0
TPC (N = 172)	172	91	39	19	11	7	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

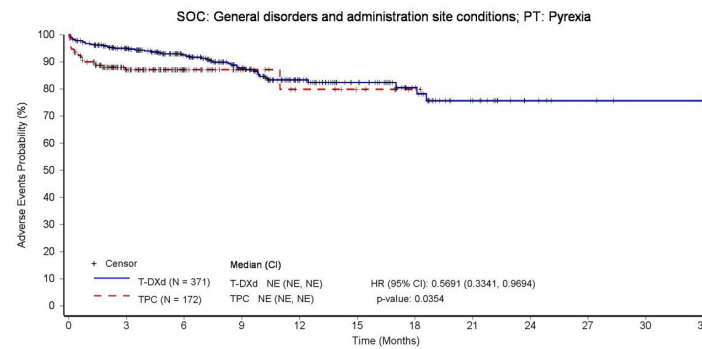
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 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf



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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

T-DXd (N = 371)	371	300	225	160	93	61	36	16	6	3	1	0
TPC (N = 172)	172	93	41	18	9	6	1	0	0	0	0	0

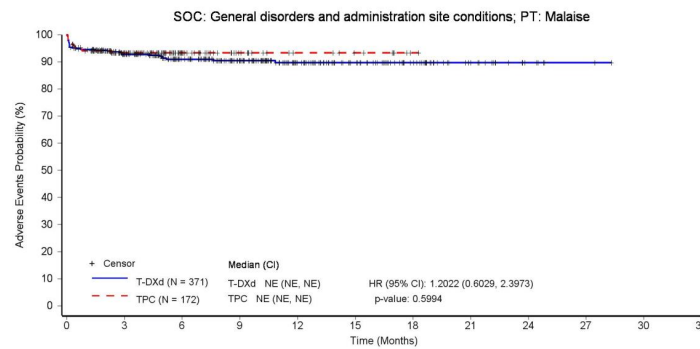
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

T-DXd (N = 371)	371	292	217	161	102	67	39	17	6	2	0	0
TPC (N = 172)	172	102	42	19	10	7	1	0	0	0	0	0

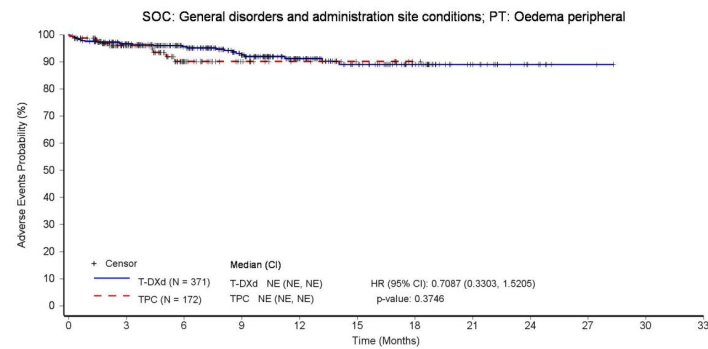
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	307	233	168	105	68	42	18	7	2	0	0
TPC (N = 172)	172	101	38	18	10	6	1	0	0	0	0	0

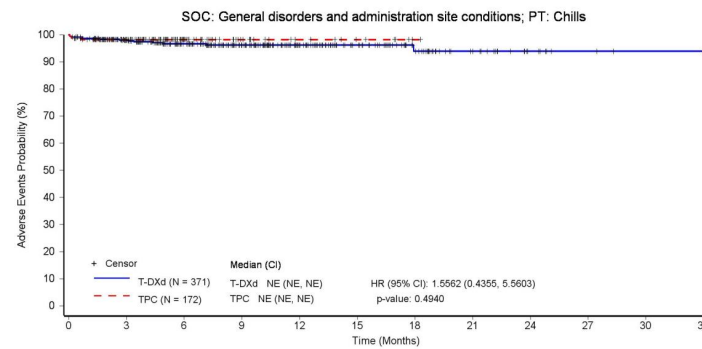
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	308	230	169	108	71	42	20	8	3	1	0
TPC (N = 172)	172	106	43	19	10	6	1	0	0	0	0	0

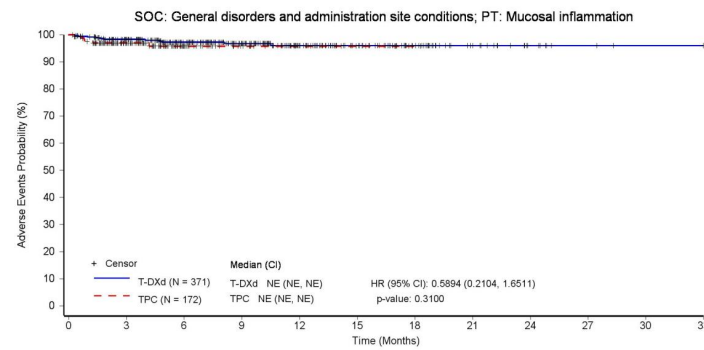
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	309	233	170	106	68	42	19	8	3	1	0
TPC (N = 172)	172	104	41	19	11	7	1	0	0	0	0	0

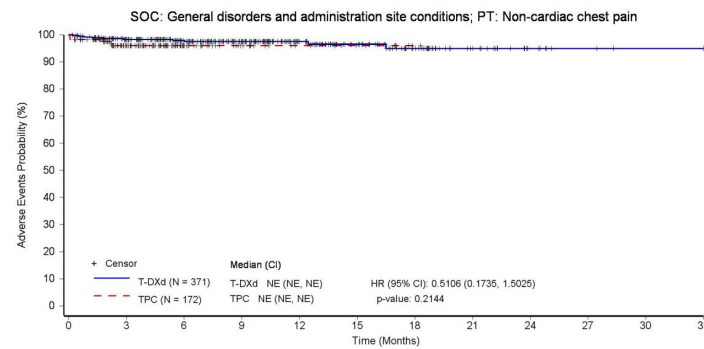
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	309	234	171	108	73	44	20	8	3	1	0
TPC (N = 172)	172	103	41	20	11	7	1	0	0	0	0	0

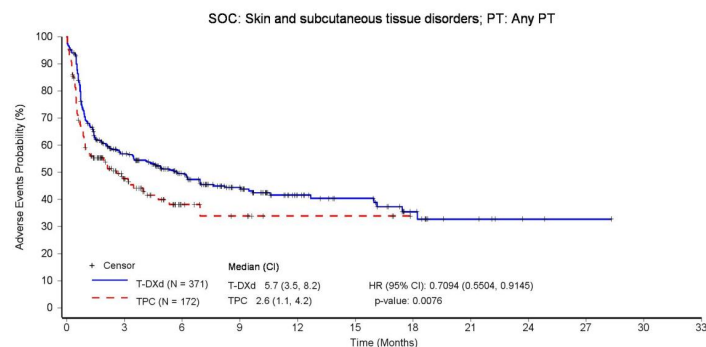
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	173	113	74	38	28	14	6	2	1	0	0
TPC (N = 172)	172	47	12	7	3	3	0	0	0	0	0	0

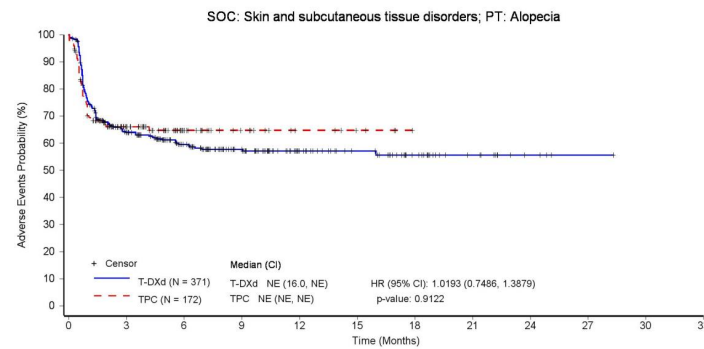
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	196	135	95	56	40	24	12	4	1	0	0
TPC (N = 172)	172	66	28	14	7	4	0	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

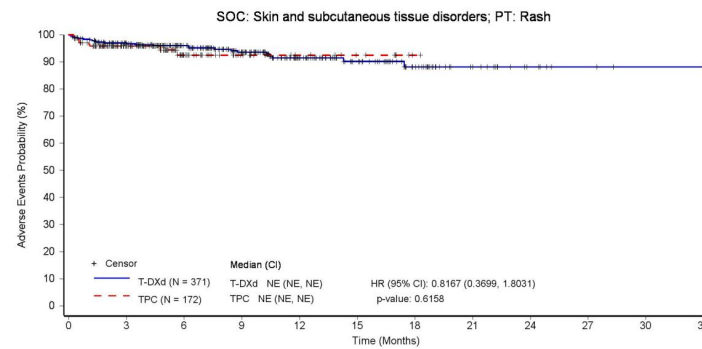
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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	305	231	167	102	65	37	16	7	3	1	0
TPC (N = 172)	172	101	40	19	11	7	1	0	0	0	0	0

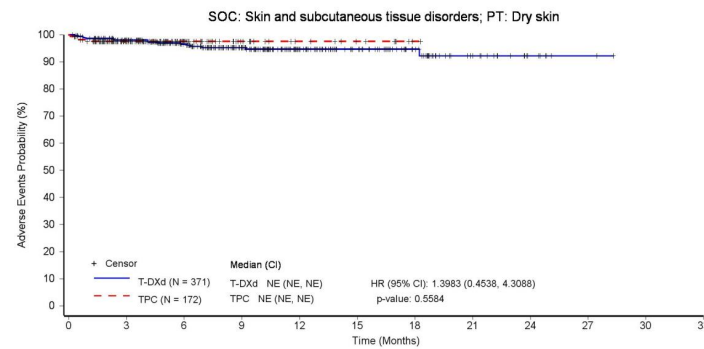
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	307	231	168	105	70	41	18	7	2	0	0
TPC (N = 172)	172	104	44	20	11	7	1	0	0	0	0	0

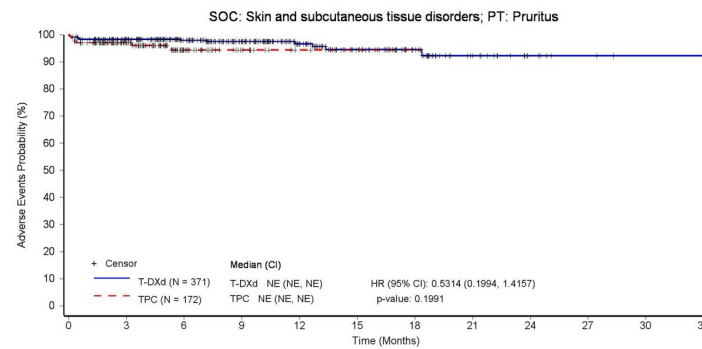
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	309	233	170	108	72	43	18	7	3	1	0
TPC (N = 172)	172	105	41	19	10	6	1	0	0	0	0	0

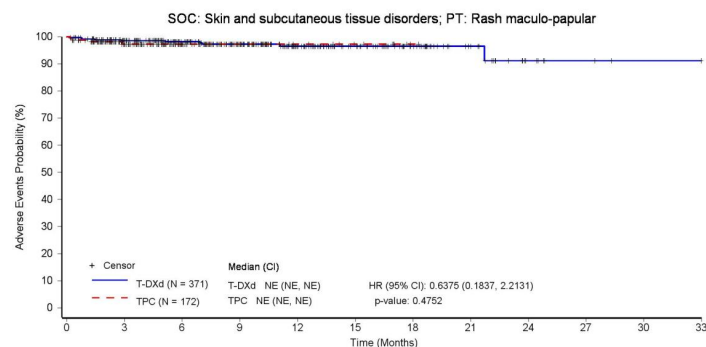
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	309	234	171	107	70	42	20	7	3	1	0
TPC (N = 172)	172	104	43	20	11	7	1	0	0	0	0	0

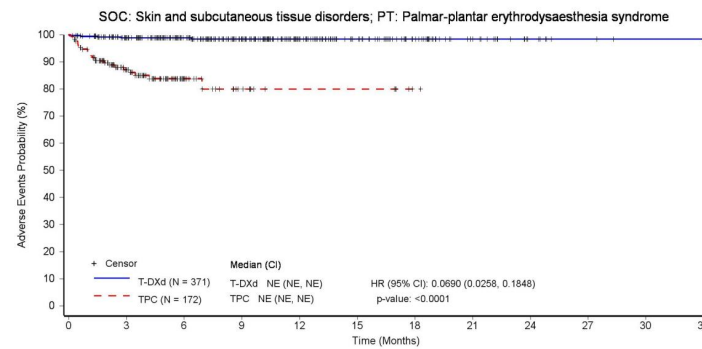
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	310	235	172	110	73	44	20	8	3	1	0
TPC (N = 172)	172	92	31	12	6	6	1	0	0	0	0	0

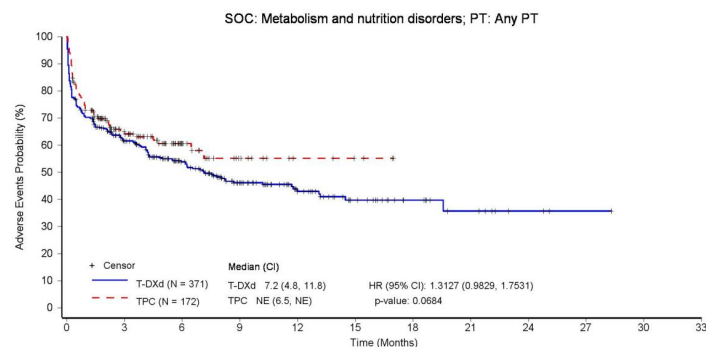
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	197	131	82	48	28	15	8	3	1	0	0
TPC (N = 172)	172	73	27	12	5	3	0	0	0	0	0	0

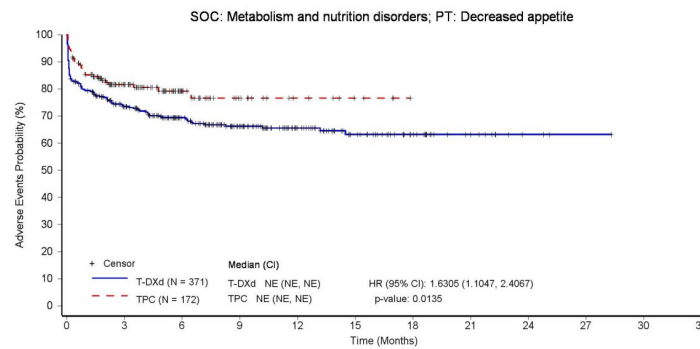
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	229	165	115	71	44	25	10	3	1	0	0
TPC (N = 172)	172	86	34	16	8	4	0	0	0	0	0	0

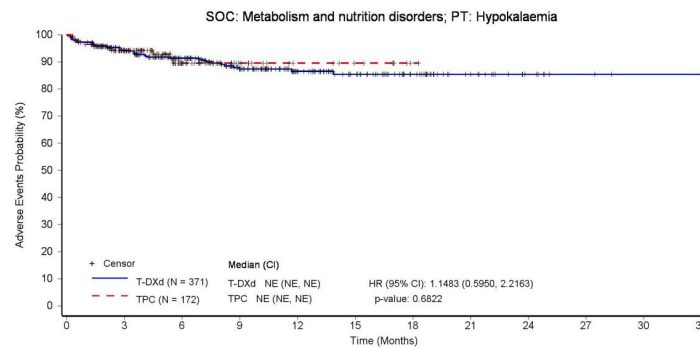
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

T-DXd (N = 371)	371	296	220	155	97	66	38	18	8	3	1	0
TPC (N = 172)	172	102	40	18	10	7	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

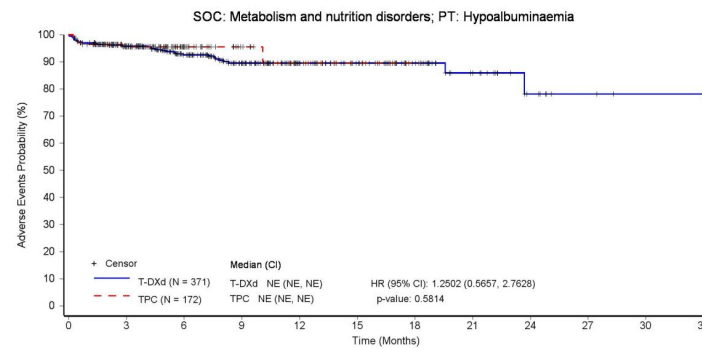
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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	303	220	157	98	66	39	19	8	3	1	0
TPC (N = 172)	172	104	42	20	11	7	1	0	0	0	0	0

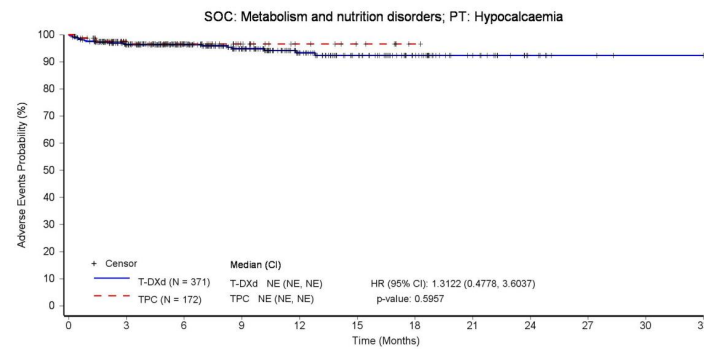
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	303	231	168	105	70	41	20	8	3	1	0
TPC (N = 172)	172	104	41	19	10	6	1	0	0	0	0	0

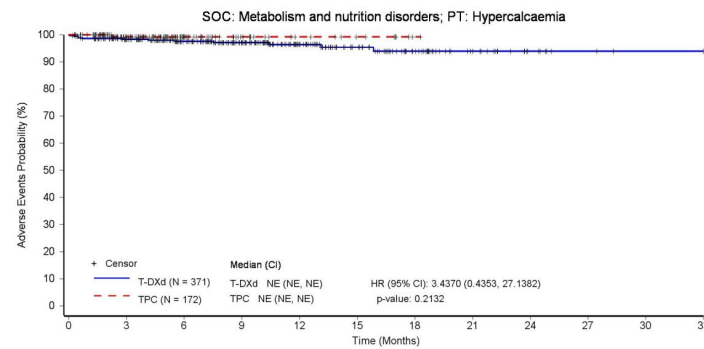
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	310	234	172	110	72	42	20	8	3	1	0
TPC (N = 172)	172	107	44	20	11	7	1	0	0	0	0	0

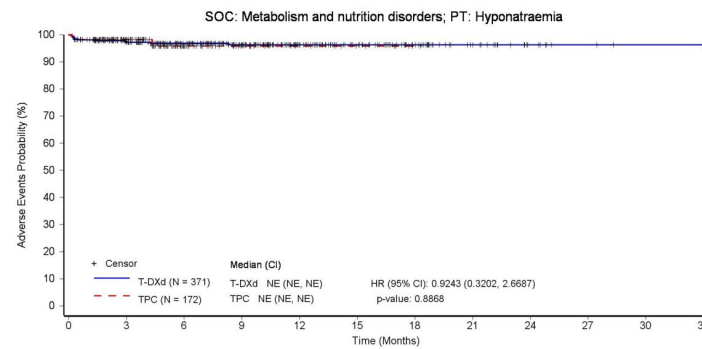
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	307	231	169	107	71	42	20	8	3	1	0
TPC (N = 172)	172	106	43	19	10	6	1	0	0	0	0	0

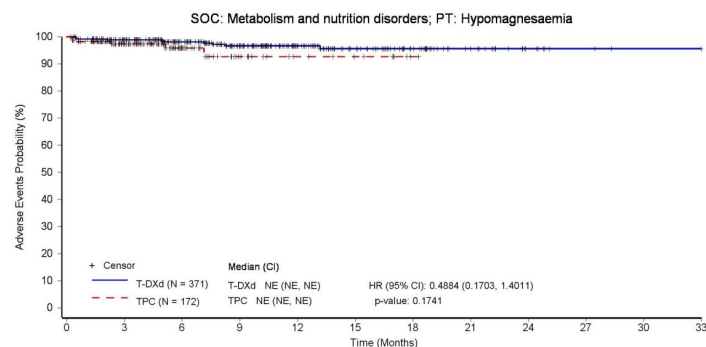
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	310	232	169	107	69	41	20	8	3	1	0
TPC (N = 172)	172	105	42	19	10	7	1	0	0	0	0	0

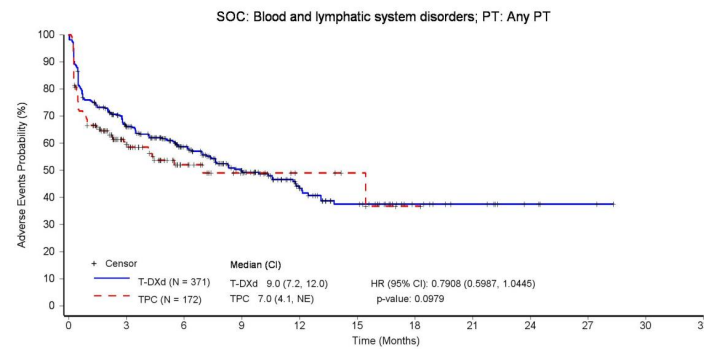
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	216	143	92	50	31	14	9	4	2	0	0
TPC (N = 172)	172	61	24	11	6	4	1	0	0	0	0	0

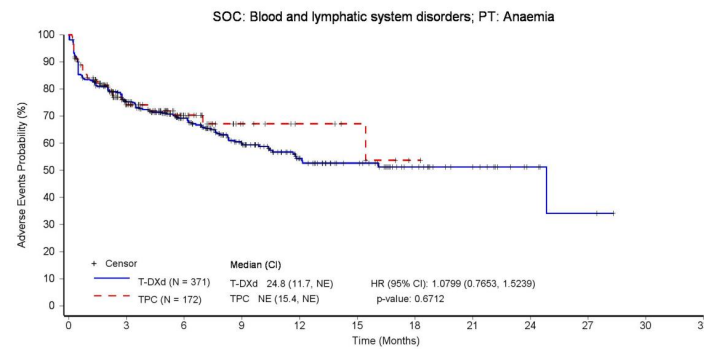
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	241	170	111	65	45	23	13	5	2	0	0
TPC (N = 172)	172	79	33	12	7	5	1	0	0	0	0	0

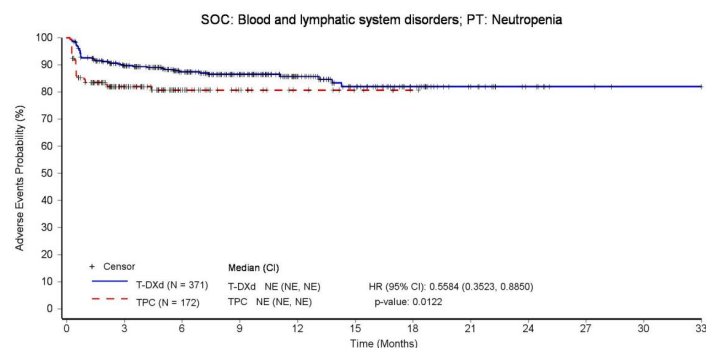
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	281	204	147	89	55	33	17	8	3	1	0
TPC (N = 172)	172	85	36	17	9	5	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

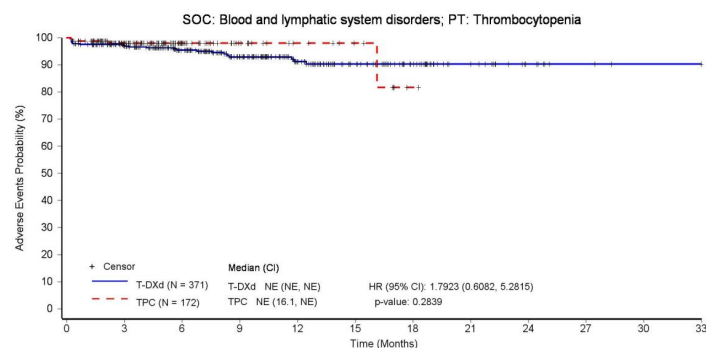
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 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf



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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	306	228	163	101	65	38	18	8	3	1	0
TPC (N = 172)	172	104	43	20	11	7	1	0	0	0	0	0

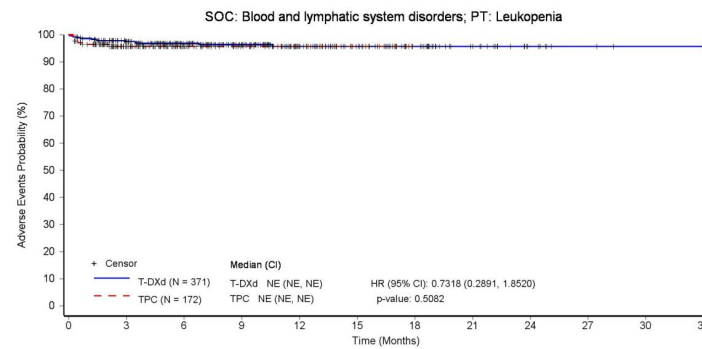
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	309	232	169	106	70	41	20	8	3	1	0
TPC (N = 172)	172	101	43	20	11	7	1	0	0	0	0	0

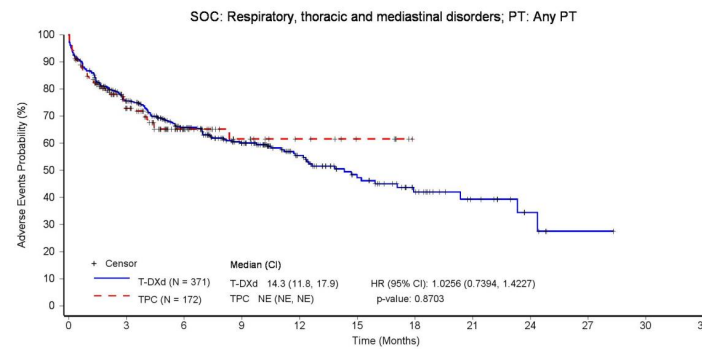
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	250	176	125	73	43	25	13	5	1	0	0
TPC (N = 172)	172	81	33	15	9	5	0	0	0	0	0	0

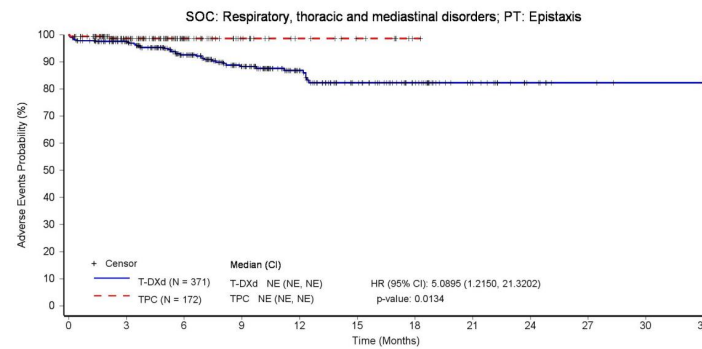
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	309	222	158	99	64	39	18	8	3	1	0
TPC (N = 172)	172	105	44	20	11	7	1	0	0	0	0	0

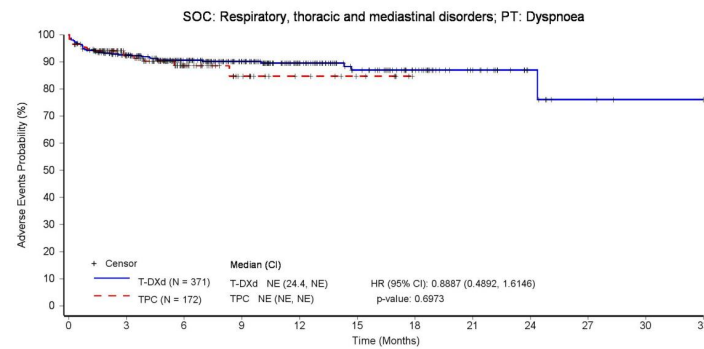
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	299	225	165	104	66	41	20	8	3	1	0
TPC (N = 172)	172	101	41	18	10	6	0	0	0	0	0	0

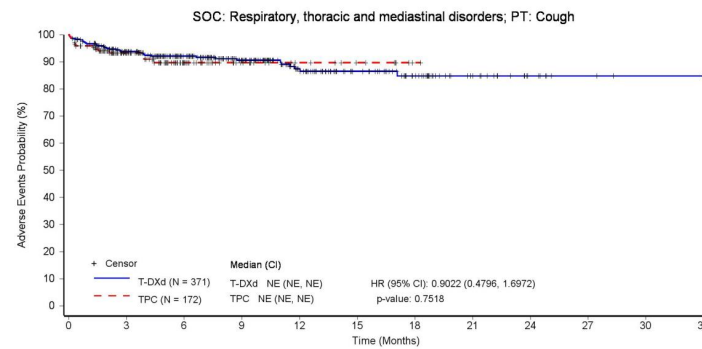
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	294	223	161	98	66	41	19	8	3	1	0
TPC (N = 172)	172	99	43	20	11	7	1	0	0	0	0	0

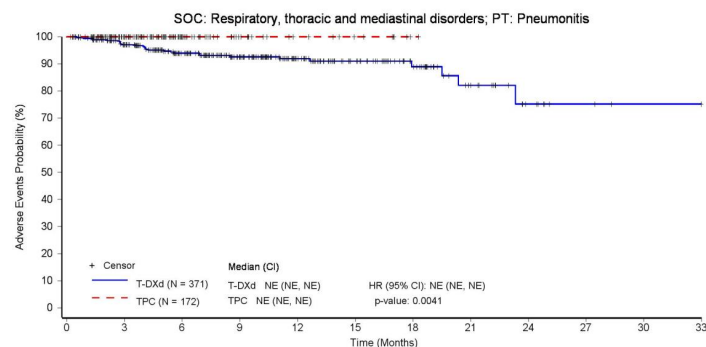
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	310	234	171	110	72	43	19	8	3	1	0
TPC (N = 172)	172	107	44	20	11	7	1	0	0	0	0	0

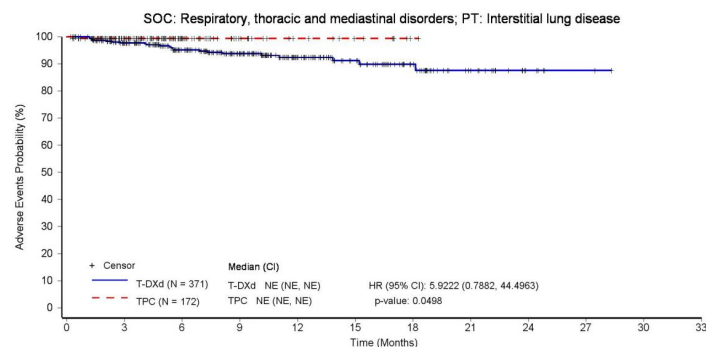
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	310	232	170	105	70	41	18	6	2	0	0
TPC (N = 172)	172	107	44	20	11	7	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

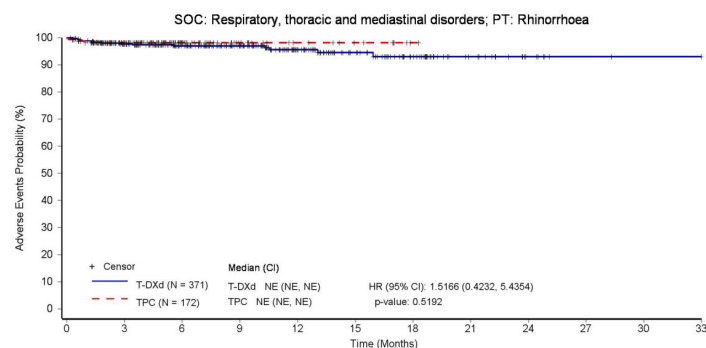
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 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf



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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	306	231	170	104	67	40	18	7	2	1	0
TPC (N = 172)	172	105	44	20	11	7	1	0	0	0	0	0

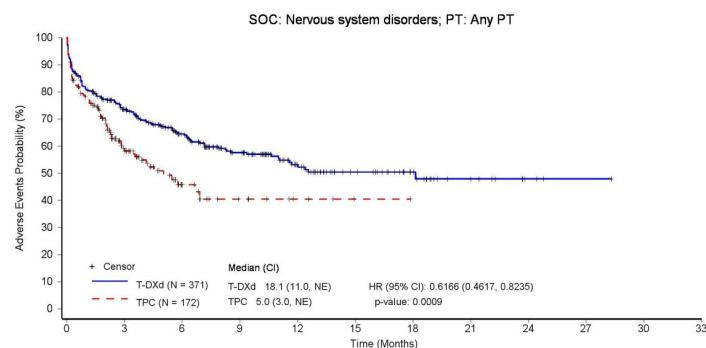
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	231	155	104	60	35	21	9	3	1	0	0
TPC (N = 172)	172	61	20	9	4	1	0	0	0	0	0	0

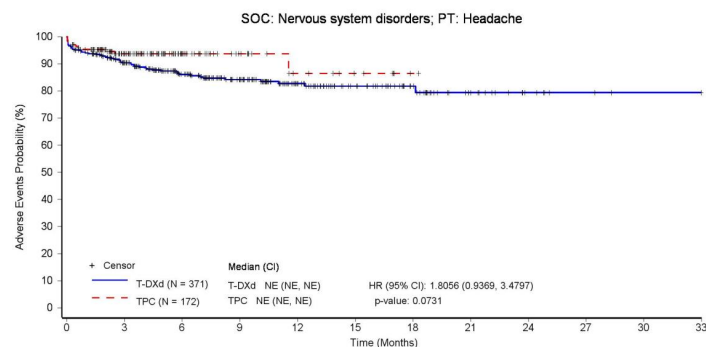
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	282	201	144	89	59	36	16	7	3	1	0
TPC (N = 172)	172	100	41	19	10	6	1	0	0	0	0	0

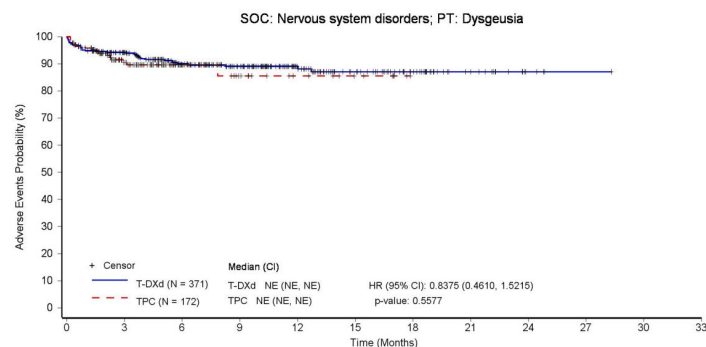
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

T-DXd (N = 371)	371	295	214	155	94	60	37	15	4	1	0	0
TPC (N = 172)	172	97	38	17	10	6	0	0	0	0	0	0

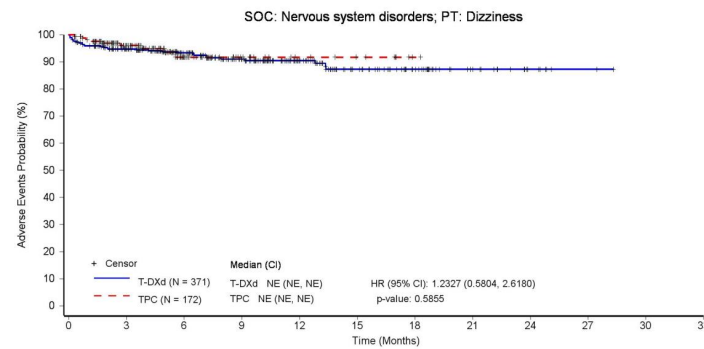
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	298	223	159	101	63	39	17	7	2	0	0
TPC (N = 172)	172	103	41	19	10	7	1	0	0	0	0	0

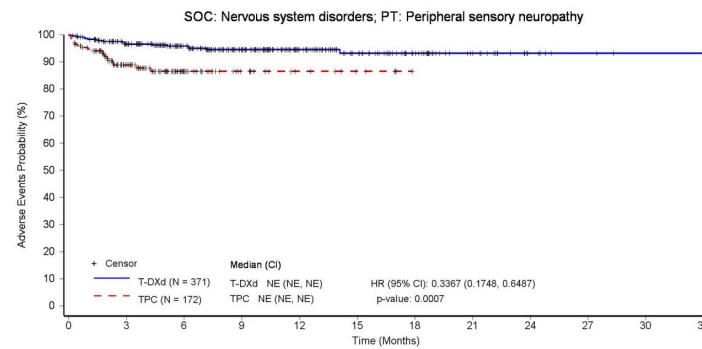
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	303	228	165	102	66	39	19	7	3	1	0
TPC (N = 172)	172	94	37	17	9	5	0	0	0	0	0	0

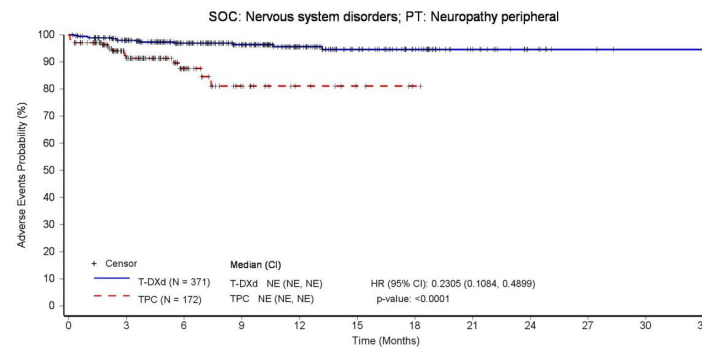
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	308	230	168	106	68	42	19	8	3	1	0
TPC (N = 172)	172	97	38	16	8	4	1	0	0	0	0	0

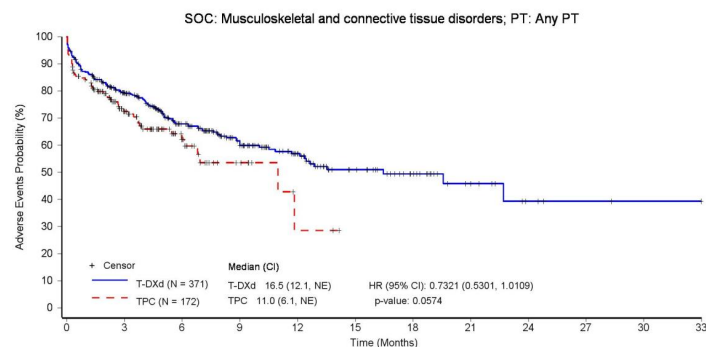
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	250	166	107	65	39	23	10	4	2	1	0
TPC (N = 172)	172	77	28	9	2	0	0	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

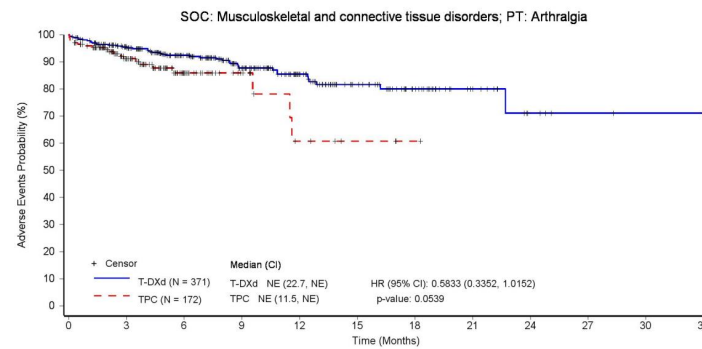
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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	300	220	153	95	59	34	14	5	2	1	0
TPC (N = 172)	172	98	35	15	6	3	1	0	0	0	0	0

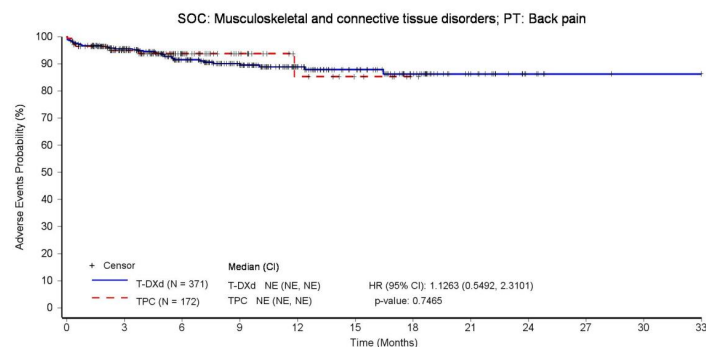
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	298	215	157	98	67	39	18	6	2	1	0
TPC (N = 172)	172	100	43	20	10	6	1	0	0	0	0	0

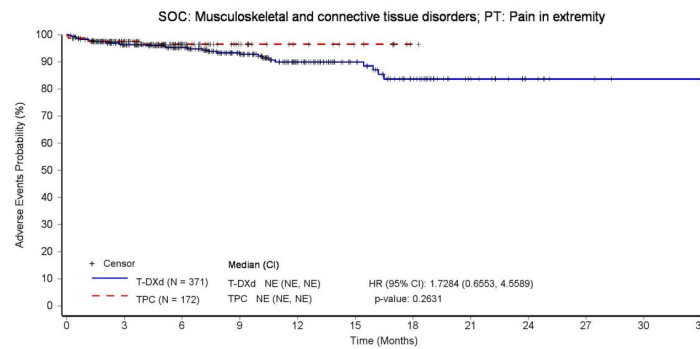
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	302	228	164	99	65	37	16	7	3	1	0
TPC (N = 172)	172	106	42	19	11	7	1	0	0	0	0	0

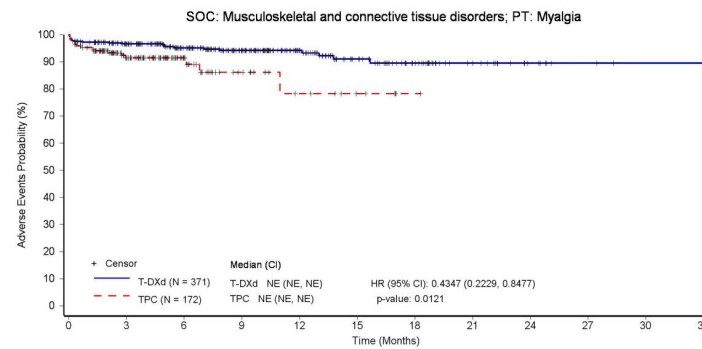
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	303	226	162	103	65	39	18	8	3	1	0
TPC (N = 172)	172	97	40	17	9	5	1	0	0	0	0	0

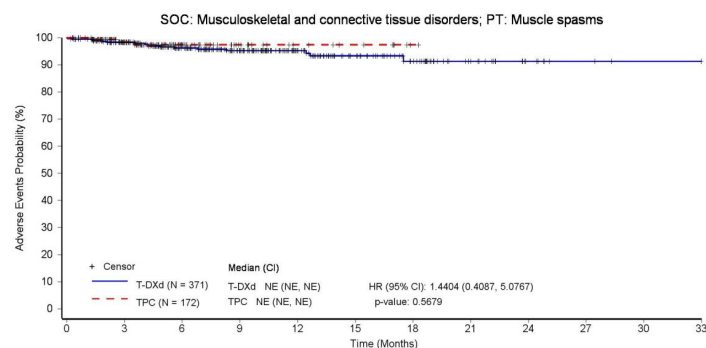
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	309	230	167	106	69	42	19	8	3	1	0
TPC (N = 172)	172	105	43	19	10	7	1	0	0	0	0	0

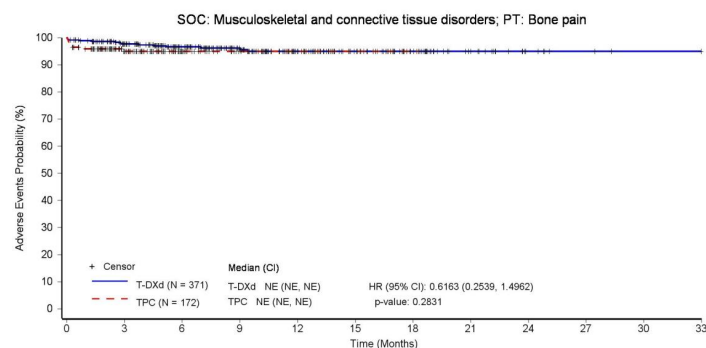
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	308	232	168	109	71	43	19	7	3	1	0
TPC (N = 172)	172	101	42	20	11	7	1	0	0	0	0	0

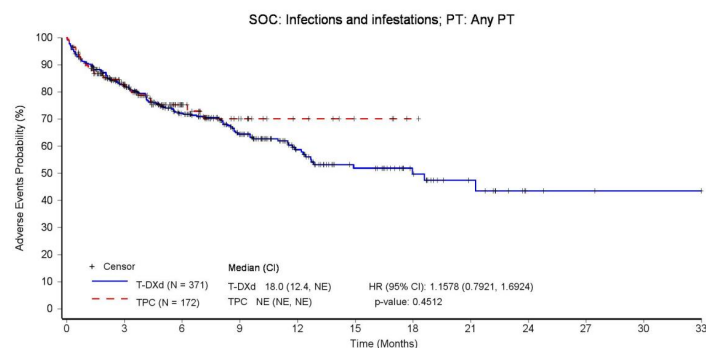
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	263	184	120	67	40	23	12	3	2	1	0
TPC (N = 172)	172	90	35	16	8	4	1	0	0	0	0	0

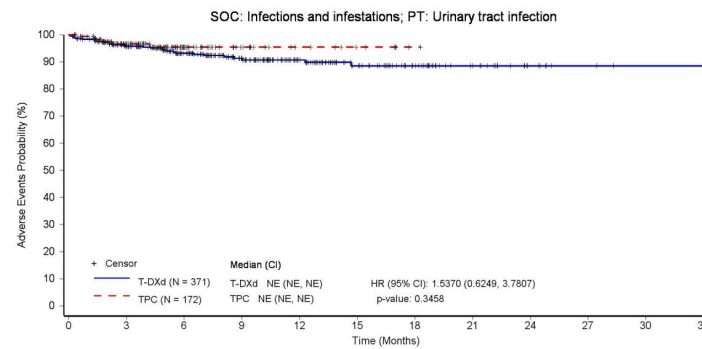
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	303	228	164	105	66	40	20	8	3	1	0
TPC (N = 172)	172	105	42	19	10	6	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

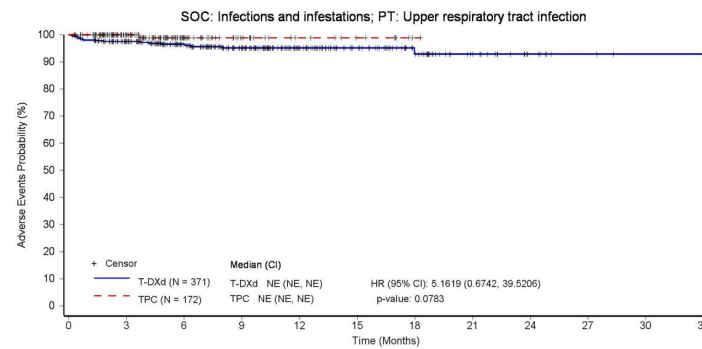
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 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf



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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	307	232	170	107	71	42	19	8	3	1	0
TPC (N = 172)	172	107	43	20	11	7	1	0	0	0	0	0

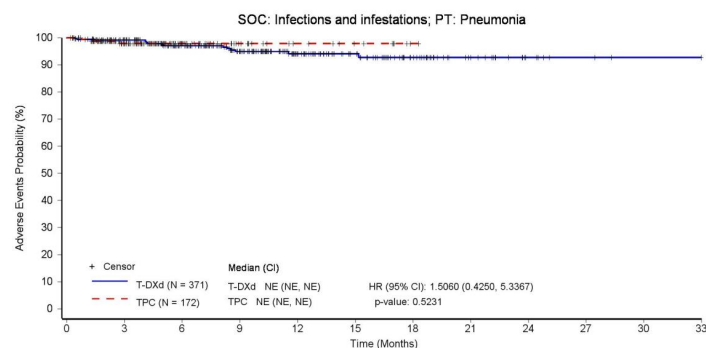
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	313	235	168	105	70	40	18	7	3	1	0
TPC (N = 172)	172	105	44	20	11	7	1	0	0	0	0	0

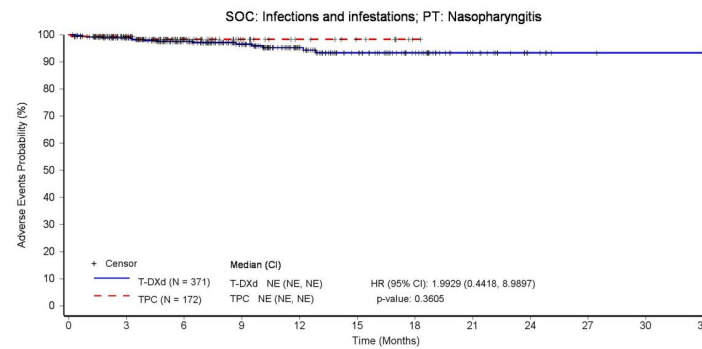
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	310	233	170	107	69	41	18	6	2	1	0
TPC (N = 172)	172	106	43	20	11	7	1	0	0	0	0	0

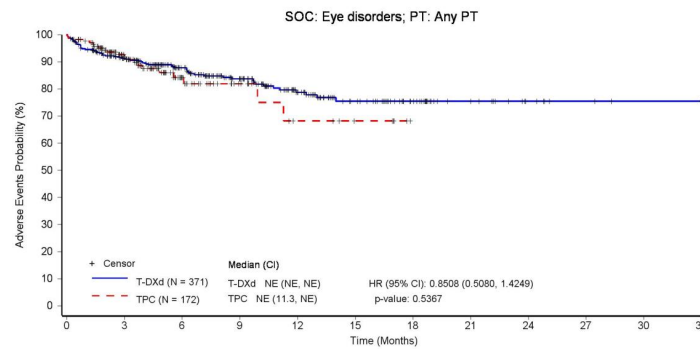
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	285	211	149	89	54	32	15	7	3	1	0
TPC (N = 172)	172	98	38	17	8	5	0	0	0	0	0	0

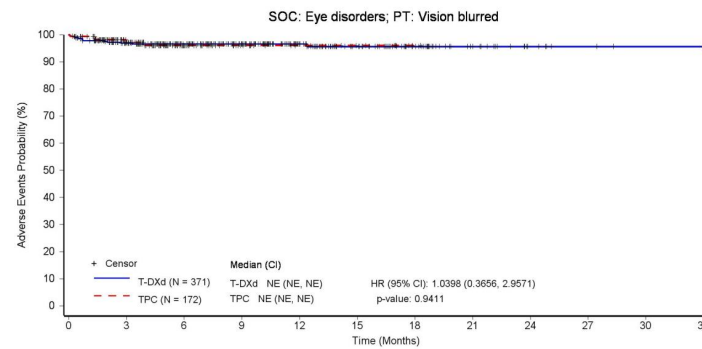
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	304	229	168	107	69	40	18	7	3	1	0
TPC (N = 172)	172	104	43	19	11	7	1	0	0	0	0	0

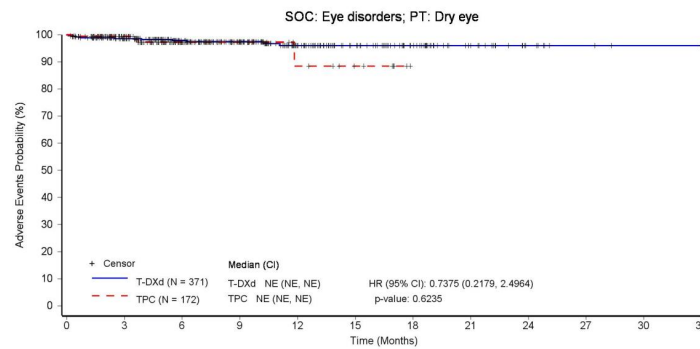
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	309	234	171	108	71	44	20	8	3	1	0
TPC (N = 172)	172	106	42	20	10	6	0	0	0	0	0	0

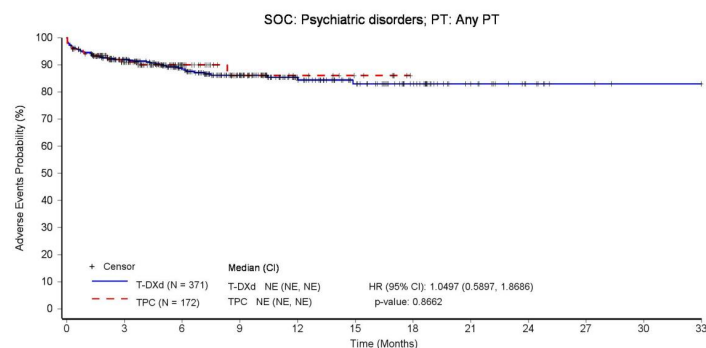
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

T-DXd (N = 371)	371	292	209	147	86	58	35	17	8	3	1	0
TPC (N = 172)	172	96	39	18	10	6	0	0	0	0	0	0

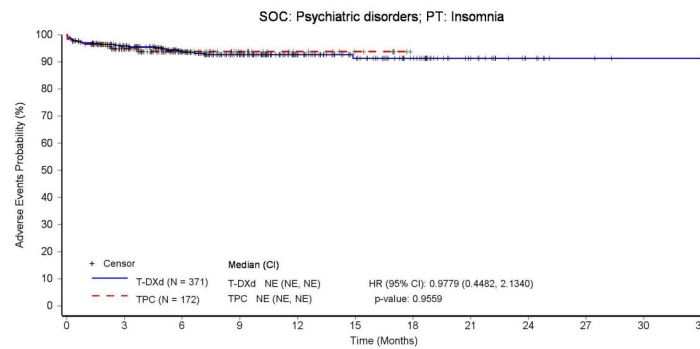
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	303	223	161	98	66	40	19	8	3	1	0
TPC (N = 172)	172	100	42	19	10	6	0	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

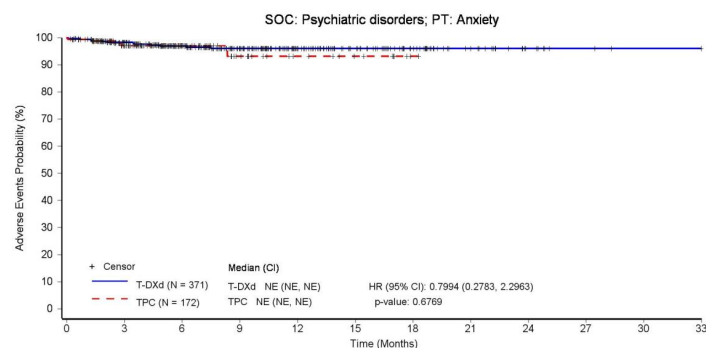
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 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf



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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	309	229	166	103	68	41	20	8	3	1	0
TPC (N = 172)	172	104	43	20	11	7	1	0	0	0	0	0

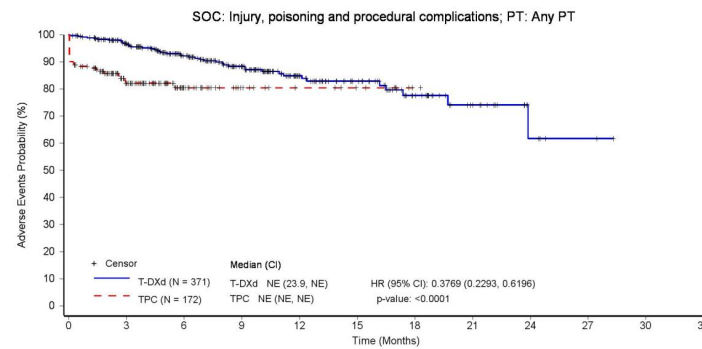
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	304	218	153	89	61	34	16	5	2	0	0
TPC (N = 172)	172	86	34	16	10	7	1	0	0	0	0	0

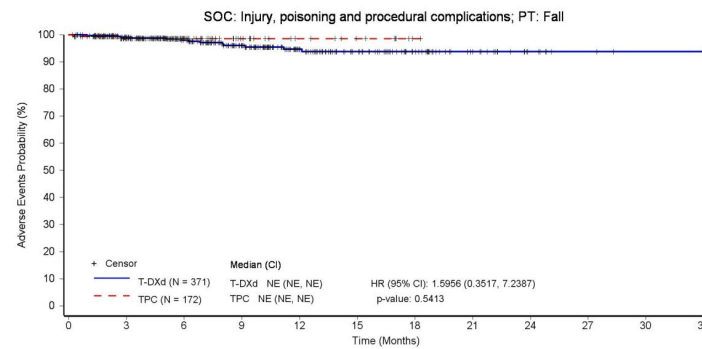
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	312	233	169	103	69	42	20	8	3	1	0
TPC (N = 172)	172	106	44	20	11	7	1	0	0	0	0	0

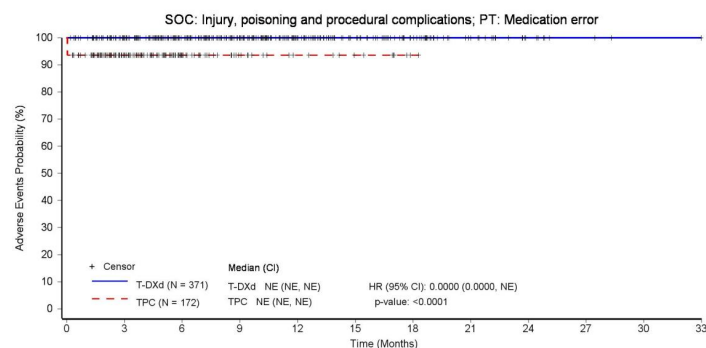
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

T-DXd (N = 371)	371	314	238	175	111	73	44	20	8	3	1	0
TPC (N = 172)	172	98	40	19	11	7	1	0	0	0	0	0

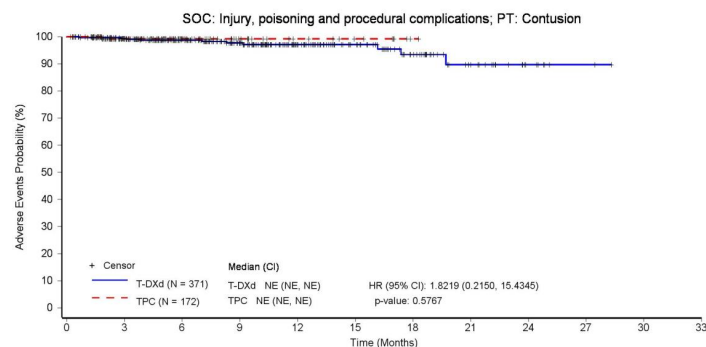
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	312	234	170	106	70	41	19	7	2	0	0
TPC (N = 172)	172	106	44	20	11	7	1	0	0	0	0	0

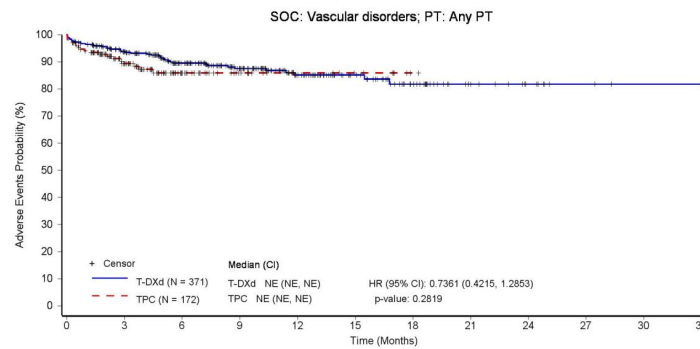
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	298	215	155	95	60	34	14	8	3	1	0
TPC (N = 172)	172	96	40	19	10	7	1	0	0	0	0	0

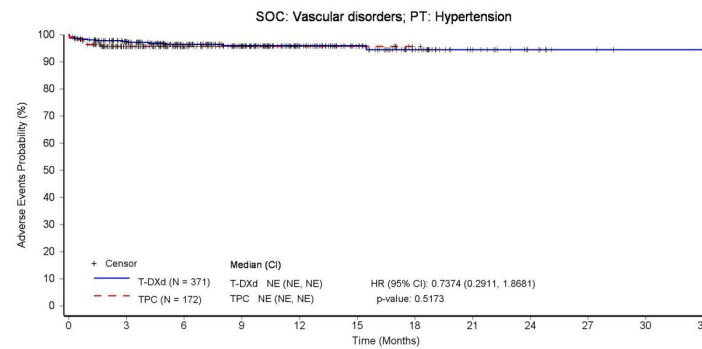
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	306	228	168	106	69	39	17	8	3	1	0
TPC (N = 172)	172	103	43	19	10	7	1	0	0	0	0	0

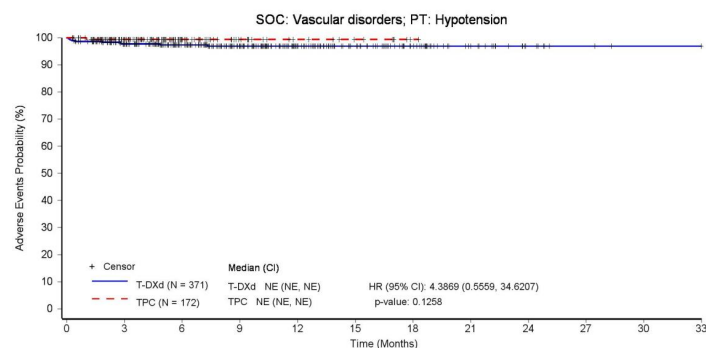
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	309	234	170	108	71	43	20	8	3	1	0
TPC (N = 172)	172	106	43	20	11	7	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

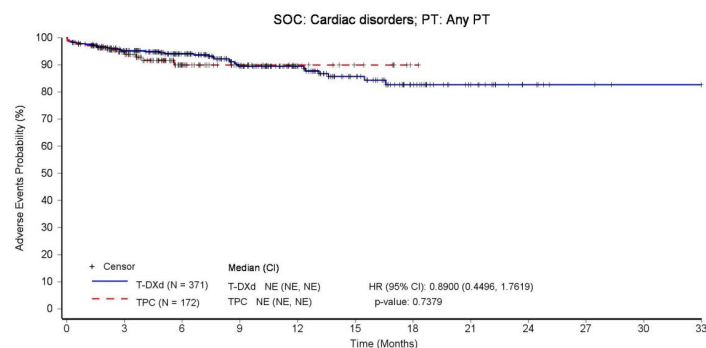
Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf



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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	303	226	160	106	66	36	17	7	3	1	0
TPC (N = 172)	172	104	40	20	11	7	1	0	0	0	0	0

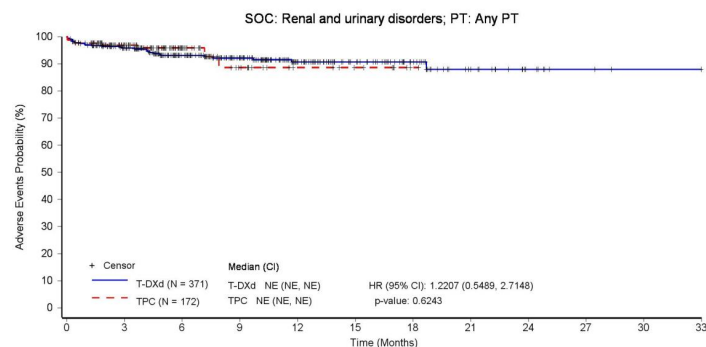
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	303	225	163	100	65	40	18	8	3	1	0
TPC (N = 172)	172	107	43	19	10	7	1	0	0	0	0	0

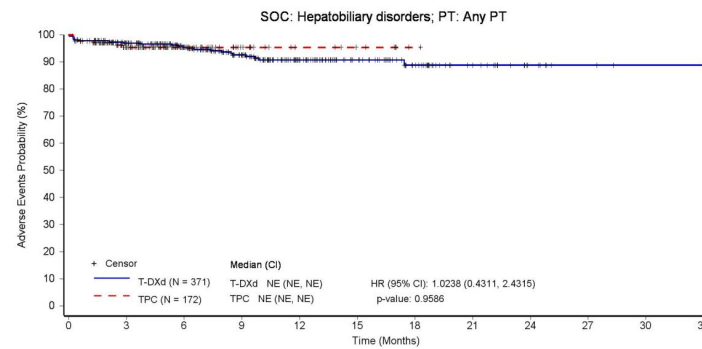
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	305	233	168	104	68	40	19	8	3	1	0
TPC (N = 172)	172	104	42	18	9	6	1	0	0	0	0	0

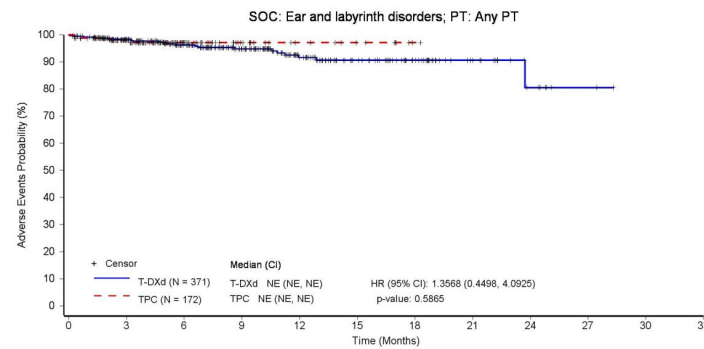
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	309	230	167	101	66	40	17	7	2	0	0
TPC (N = 172)	172	107	44	20	11	7	1	0	0	0	0	0

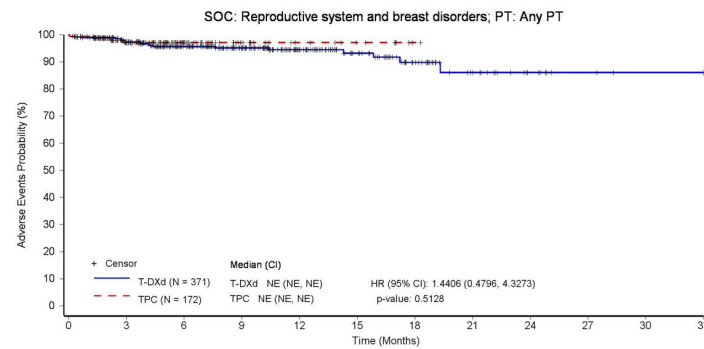
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.3 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	306	228	168	105	69	39	18	8	3	1	0
TPC (N = 172)	172	107	44	20	11	7	1	0	0	0	0	0

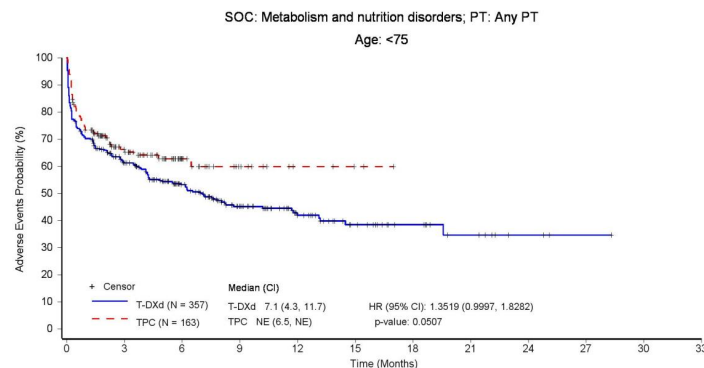
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:25; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESOCPT10PAT\_3\_SAS.rf

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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 357)	357	188	124	78	45	26	15	8	3	1	0	0
TPC (N = 163)	163	69	25	11	4	2	0	0	0	0	0	0

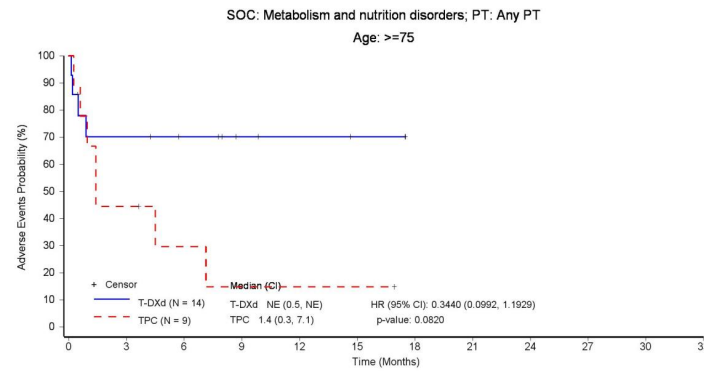
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:32; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PAT\_4\_SAS.rf

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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

T-DXd (N = 14)	14	9	7	4	3	2	0	0	0	0	0	0
TPC (N = 9)	9	4	2	1	1	1	0	0	0	0	0	0

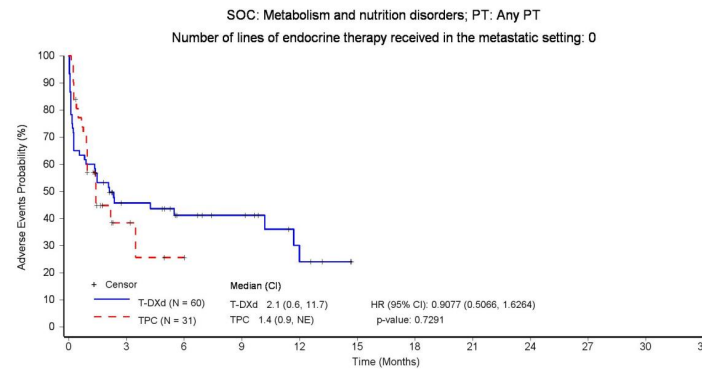
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 60)	60	22	14	11	4	0	0	0	0	0	0	0
TPC (N = 31)	31	4	1	0	0	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

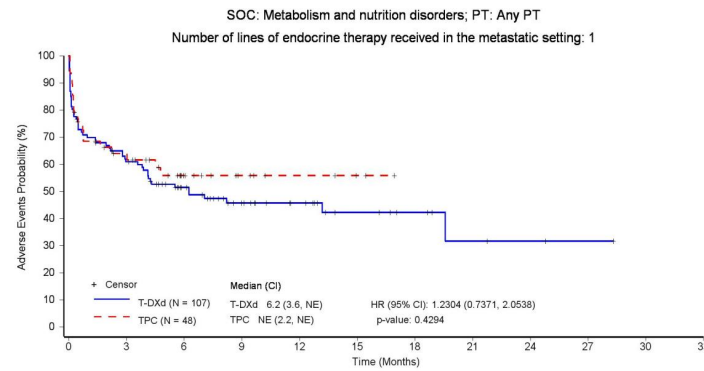
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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 107)	107	60	39	25	17	10	6	3	2	1	0	0
TPC (N = 48)	48	27	13	7	4	2	0	0	0	0	0	0

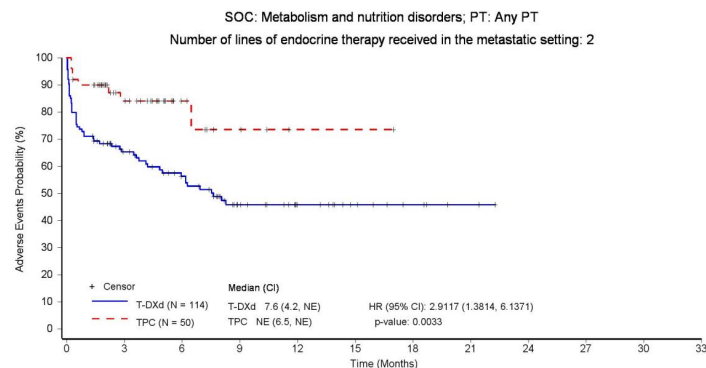
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 114)	114	61	46	26	16	9	5	2	0	0	0	0
TPC (N = 50)	50	27	9	4	1	1	0	0	0	0	0	0

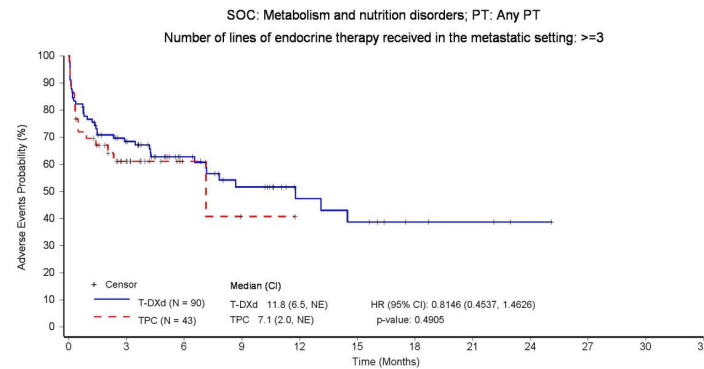
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 90)	90	54	32	20	11	9	4	3	1	0	0	0
TPC (N = 43)	43	15	4	1	0	0	0	0	0	0	0	0

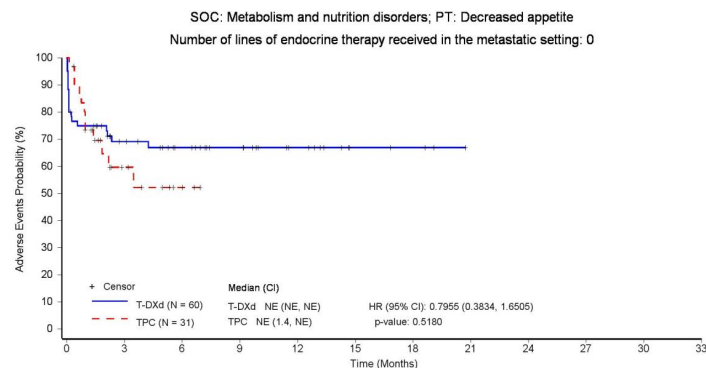
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 60)	60	33	24	18	11	4	3	0	0	0	0	0
TPC (N = 31)	31	9	3	0	0	0	0	0	0	0	0	0

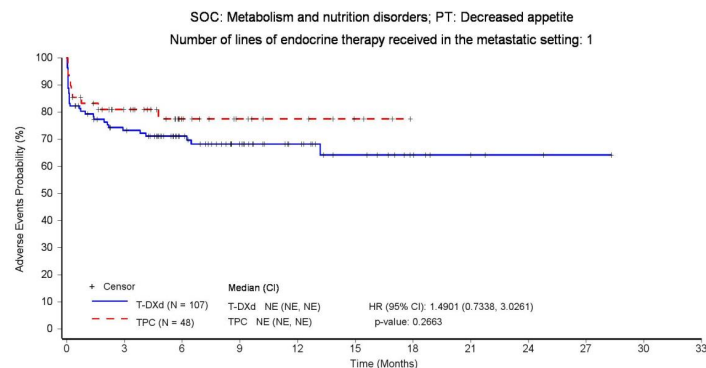
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Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 107)	107	70	50	34	22	14	7	3	2	1	0	0
TPC (N = 48)	48	30	15	9	6	3	0	0	0	0	0	0

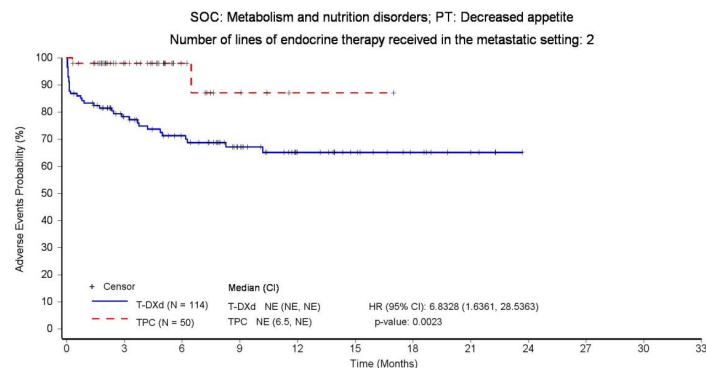
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 114)	114	70	56	38	23	15	9	4	0	0	0	0
TPC (N = 50)	50	29	10	4	1	1	0	0	0	0	0	0

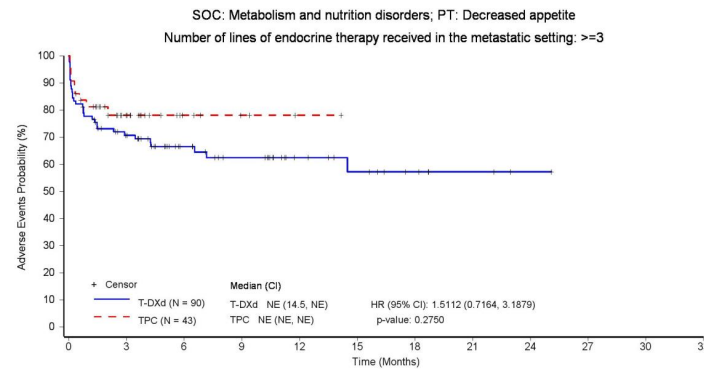
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 90)	90	56	35	25	15	11	6	3	1	0	0	0
TPC (N = 43)	43	18	6	3	1	0	0	0	0	0	0	0

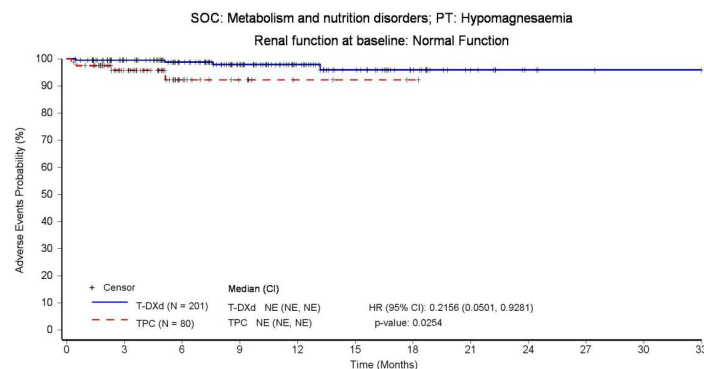
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 201)	201	171	126	93	58	39	23	10	4	2	1	0
TPC (N = 80)	80	48	16	8	3	2	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

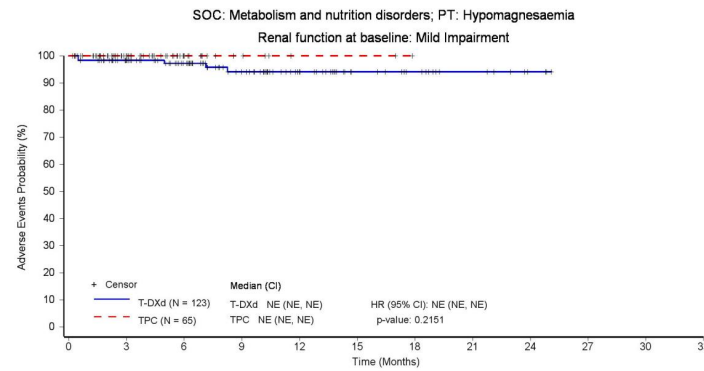
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 123)	123	101	78	55	35	20	14	8	3	0	0	0
TPC (N = 65)	65	38	15	6	2	2	0	0	0	0	0	0

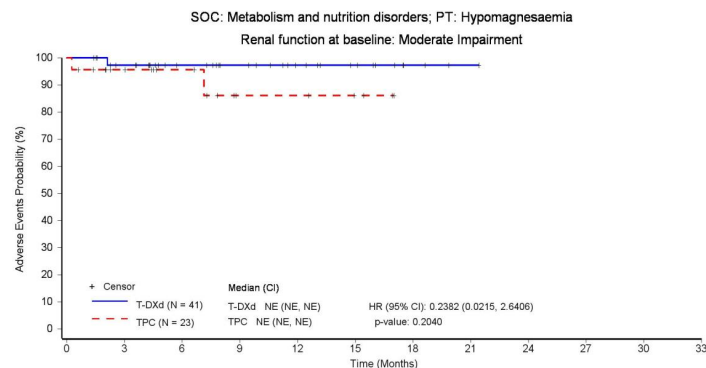
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 41)	41	34	25	19	13	9	3	1	0	0	0	0
TPC (N = 23)	23	17	11	5	5	3	0	0	0	0	0	0

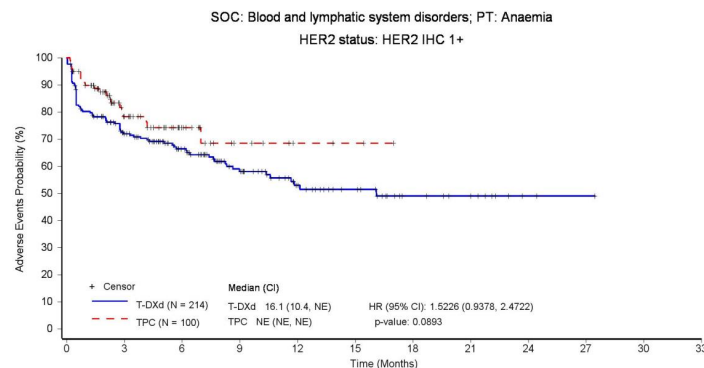
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Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 214)	214	131	93	62	37	26	13	8	2	1	0	0
TPC (N = 100)	100	45	21	7	3	2	0	0	0	0	0	0

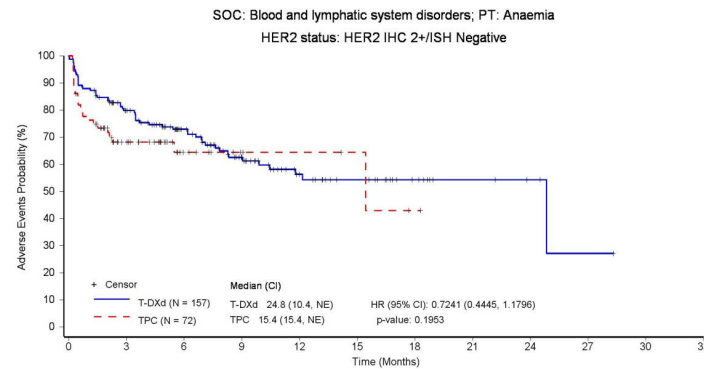
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 157)	157	110	77	49	28	19	10	5	3	1	0	0
TPC (N = 72)	72	34	12	5	4	3	1	0	0	0	0	0

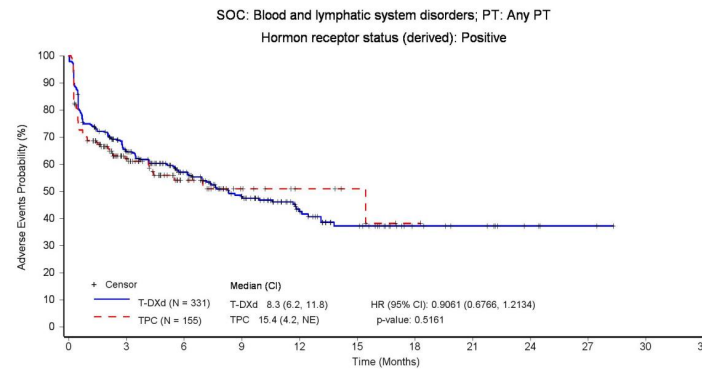
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 331)	331	191	130	83	46	28	12	9	4	2	0	0
TPC (N = 155)	155	60	23	11	6	4	1	0	0	0	0	0

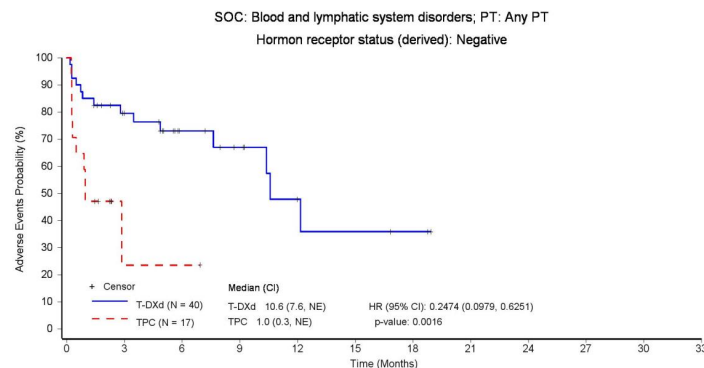
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 40)	40	25	13	9	4	3	2	0	0	0	0	0
TPC (N = 17)	17	1	1	0	0	0	0	0	0	0	0	0

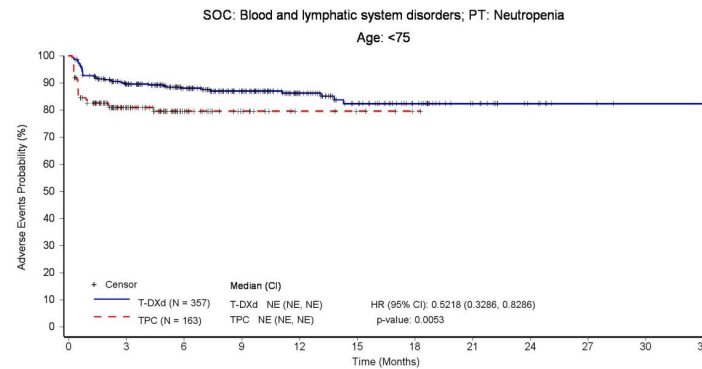
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 357)	357	270	197	143	87	54	33	17	8	3	1	0
TPC (N = 163)	163	77	31	14	6	4	1	0	0	0	0	0

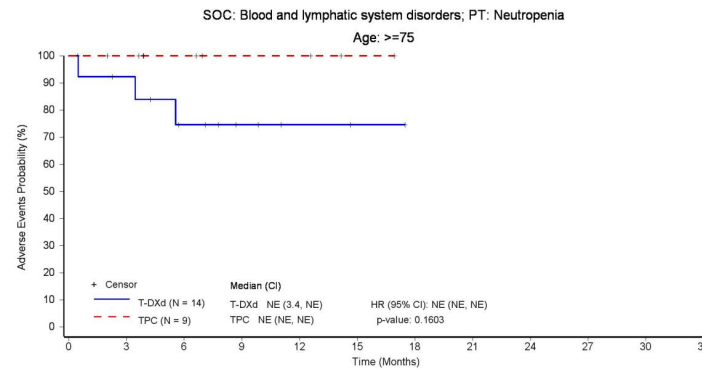
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 14)	14	11	7	4	2	1	0	0	0	0	0	0
TPC (N = 9)	9	8	5	3	3	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

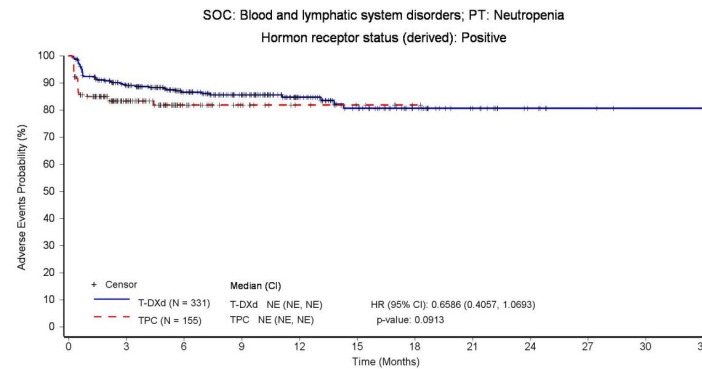
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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 331)	331	252	185	136	83	51	30	16	7	3	1	0
TPC (N = 155)	155	79	33	17	9	5	1	0	0	0	0	0

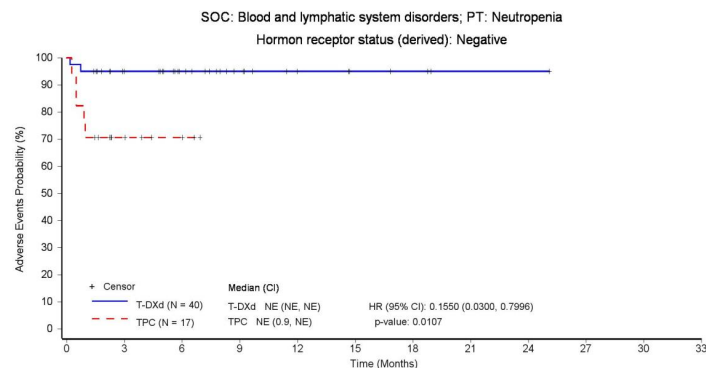
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 40)	40	29	19	11	6	4	3	1	1	0	0	0
TPC (N = 17)	17	6	3	0	0	0	0	0	0	0	0	0

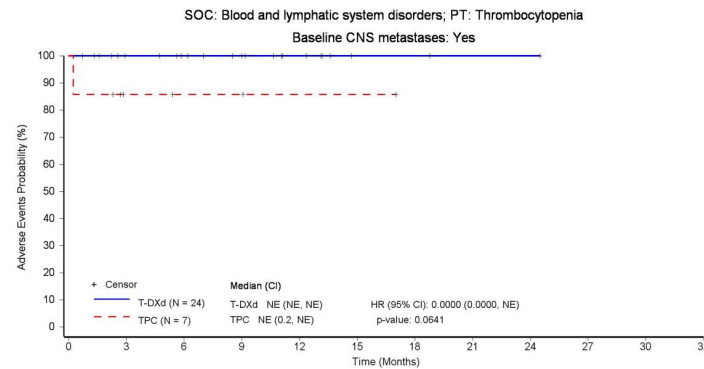
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 24)	24	18	15	12	7	2	2	1	1	0	0	0
TPC (N = 7)	7	3	2	2	1	1	0	0	0	0	0	0

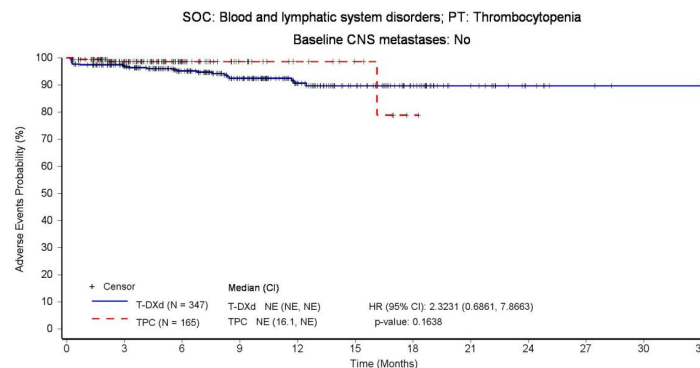
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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	T-DXd (N = 347)	TPC (N = 165)
0	347	165
3	288	101
6	213	41
9	151	18
12	94	10
15	63	6
16	36	1
18	17	0
21	7	0
24	3	0
27	1	0
30	0	0
33	0	0

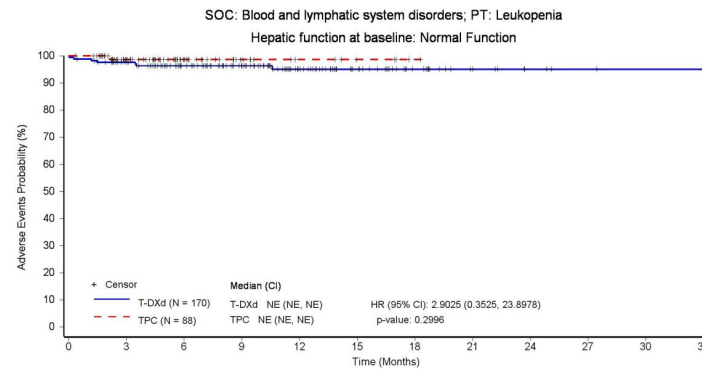
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 170)	170	153	122	95	59	37	19	8	4	2	1	0
TPC (N = 88)	88	60	28	13	7	4	1	0	0	0	0	0

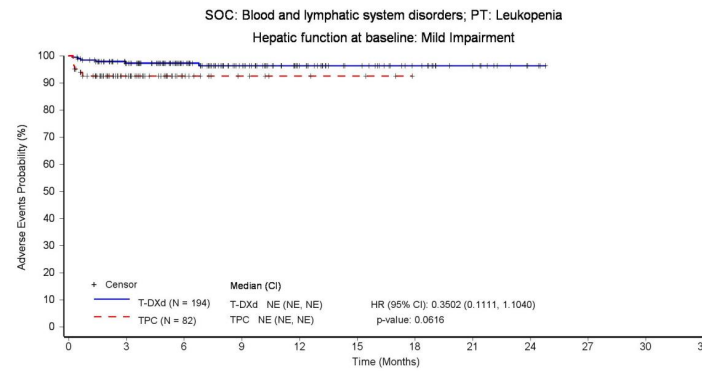
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 194)	194	153	108	72	46	32	21	11	3	0	0	0
TPC (N = 82)	82	41	15	7	4	3	0	0	0	0	0	0

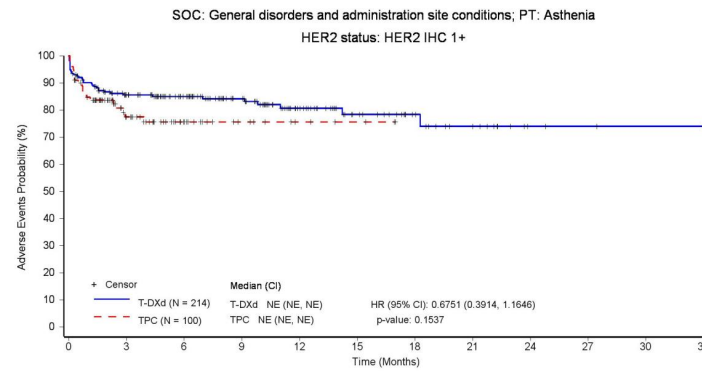
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 214)	214	152	116	86	51	30	19	11	3	2	1	0
TPC (N = 100)	100	46	22	10	5	3	0	0	0	0	0	0

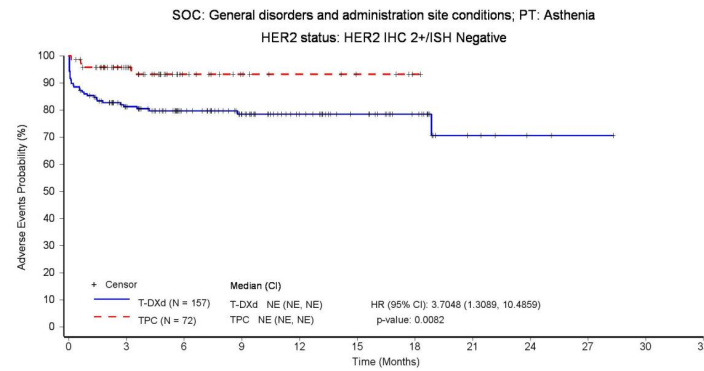
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 157)	157	109	80	60	39	27	17	5	2	1	0	0
TPC (N = 72)	72	45	17	9	6	4	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

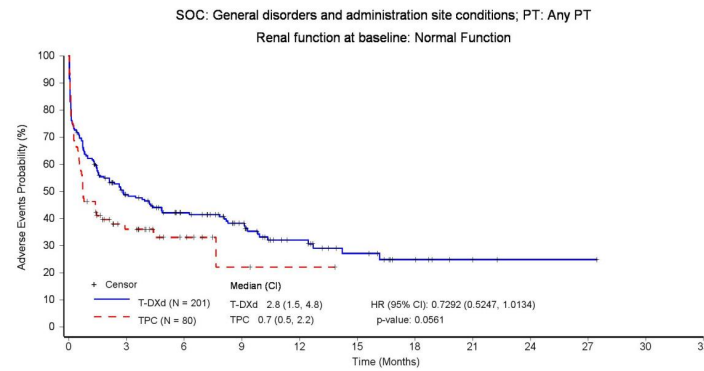
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 201)	201	84	61	43	23	14	7	2	1	1	0	0
TPC (N = 80)	80	19	8	2	1	0	0	0	0	0	0	0

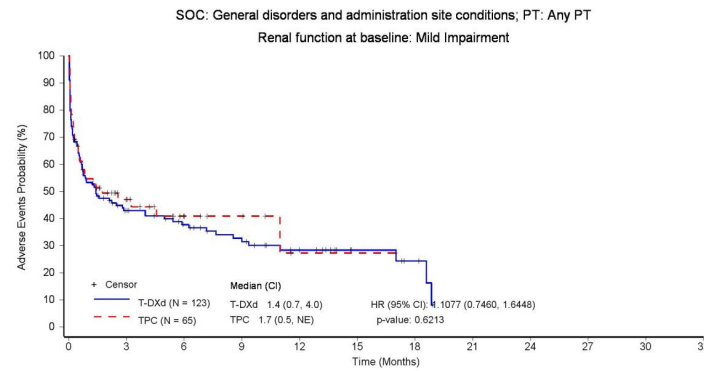
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 123)	123	45	33	25	15	7	4	0	0	0	0	0
TPC (N = 65)	65	19	8	5	1	1	0	0	0	0	0	0

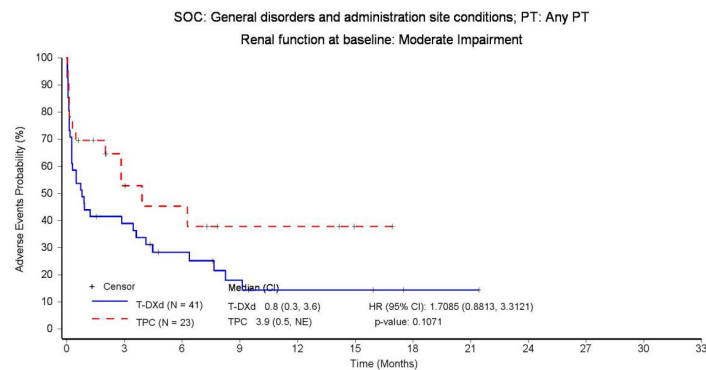
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

T-DXd (N = 41)	41	15	9	5	3	3	1	1	0	0	0	0
TPC (N = 23)	23	9	6	3	3	1	0	0	0	0	0	0

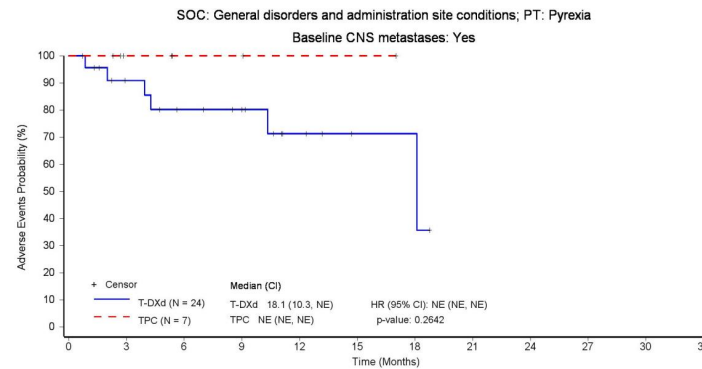
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 24)	24	17	13	11	5	2	2	0	0	0	0	0
TPC (N = 7)	7	4	2	2	1	1	0	0	0	0	0	0

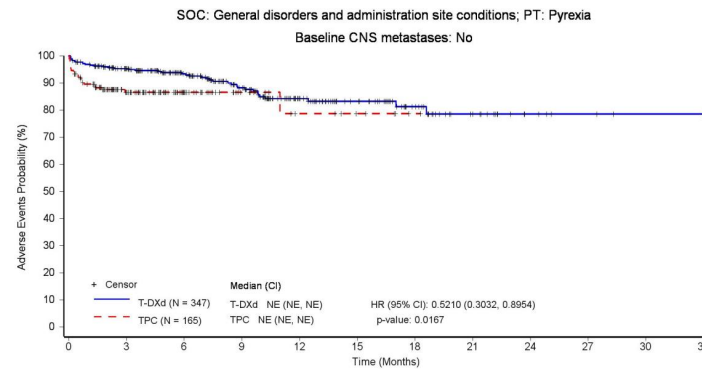
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

Time (Months)	T-DXd (N = 347)	TPC (N = 165)
0	347	165
3	283	89
6	212	39
9	149	16
12	88	8
15	59	5
18	34	1
21	16	0
24	6	0
27	3	0
30	1	0
33	0	0

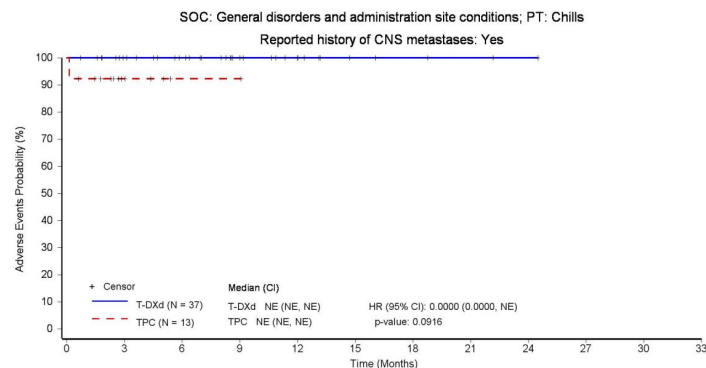
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 37)	37	30	24	15	9	4	3	2	1	0	0	0
TPC (N = 13)	13	5	1	1	0	0	0	0	0	0	0	0

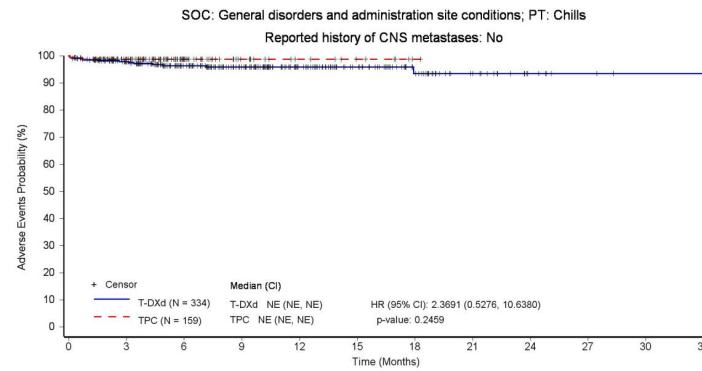
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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 334)	334	278	206	154	99	67	39	18	7	3	1	0
TPC (N = 159)	159	101	42	18	10	6	1	0	0	0	0	0

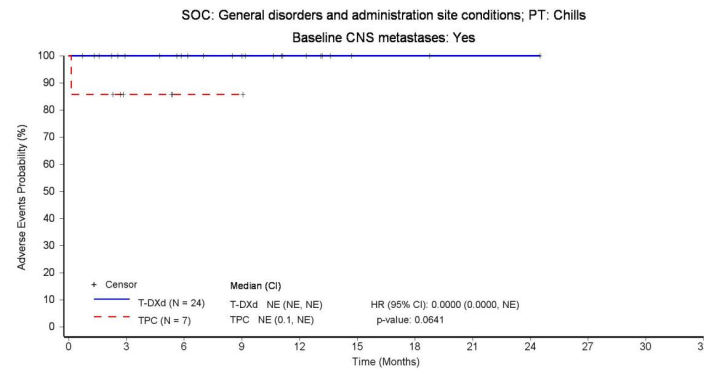
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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 24)	24	18	15	12	7	2	2	1	1	0	0	0
TPC (N = 7)	7	3	1	1	0	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

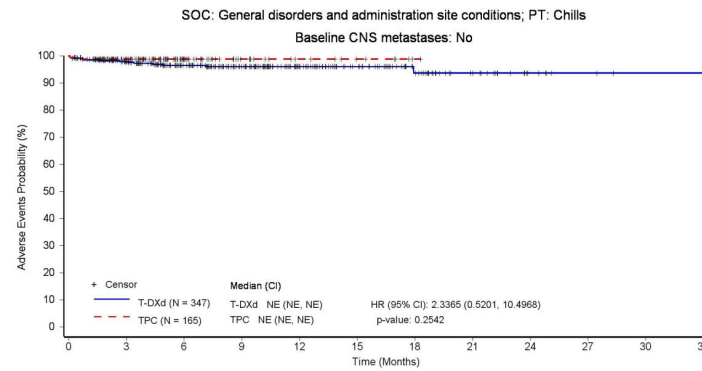
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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 347)	347	290	215	157	101	69	40	19	7	3	1	0
TPC (N = 165)	165	103	42	18	10	6	1	0	0	0	0	0

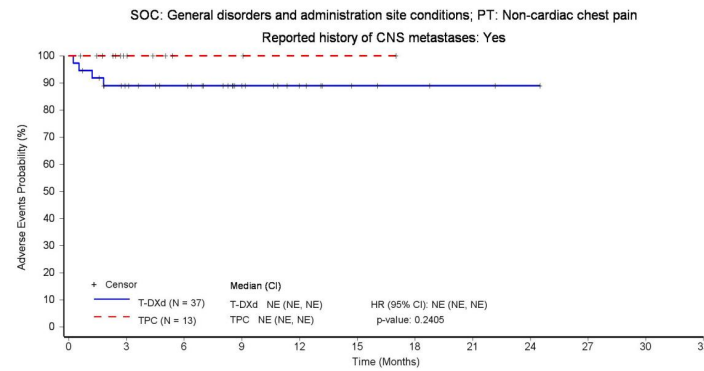
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 37)	37	27	23	14	8	4	3	2	1	0	0	0
TPC (N = 13)	13	6	2	2	1	1	0	0	0	0	0	0

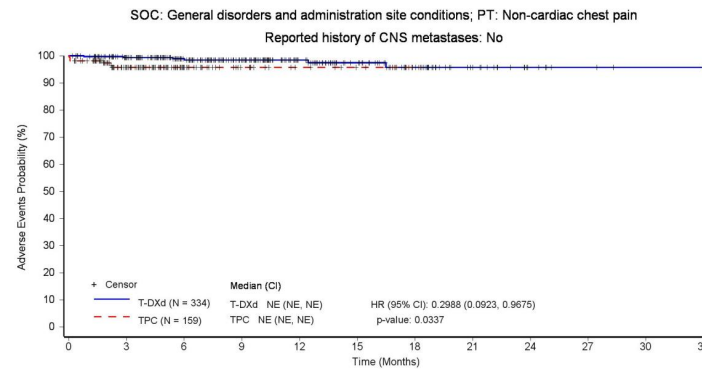
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 334)	334	282	211	157	100	69	41	18	7	3	1	0
TPC (N = 159)	159	97	39	18	10	6	1	0	0	0	0	0

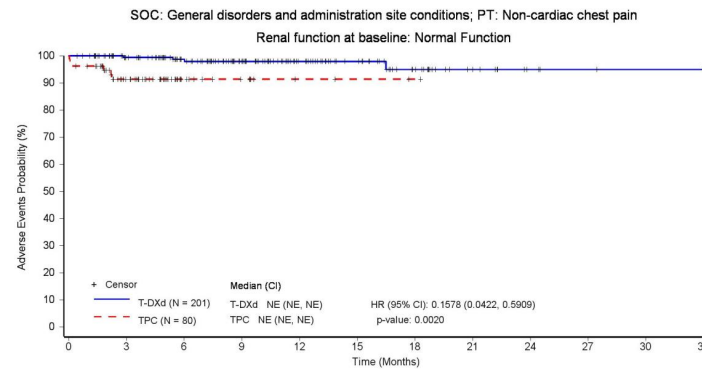
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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 201)	201	171	126	93	58	41	24	10	4	2	1	0
TPC (N = 80)	80	45	15	8	3	2	1	0	0	0	0	0

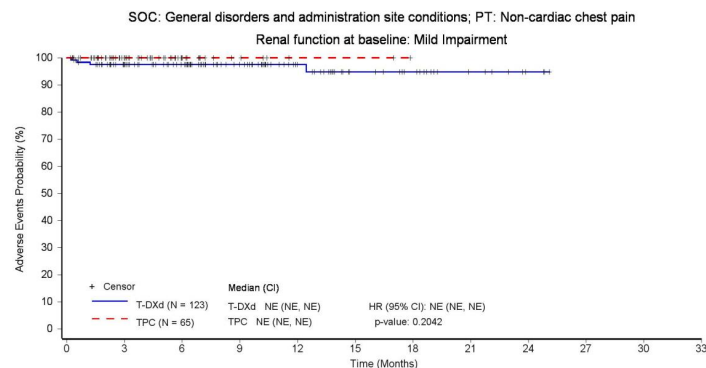
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Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 123)	123	100	80	57	36	22	16	8	3	0	0	0
TPC (N = 65)	65	38	15	6	2	2	0	0	0	0	0	0

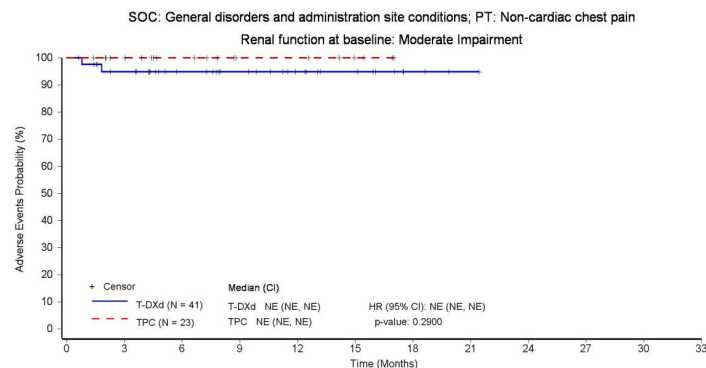
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 41)	41	34	25	19	13	9	3	1	0	0	0	0
TPC (N = 23)	23	18	11	6	6	3	0	0	0	0	0	0

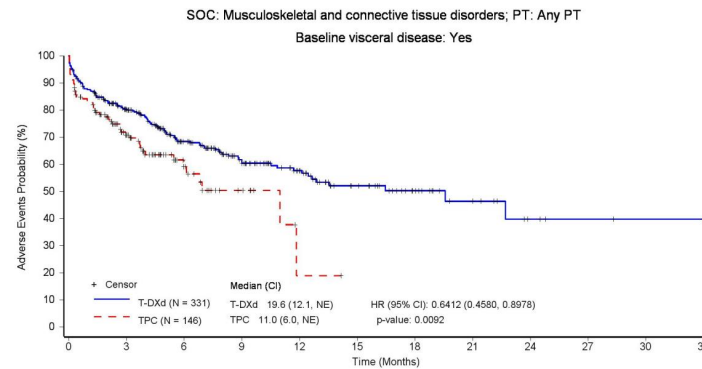
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 331)	331	223	144	93	58	35	20	10	4	2	1	0
TPC (N = 146)	146	66	23	8	1	0	0	0	0	0	0	0

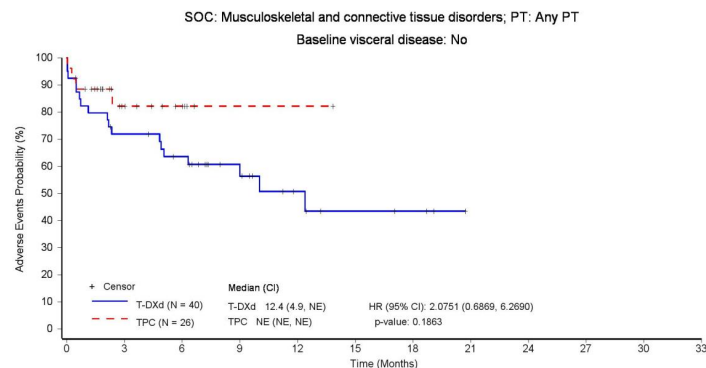
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 40)	40	27	22	14	7	4	3	0	0	0	0	0
TPC (N = 26)	26	11	5	1	1	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

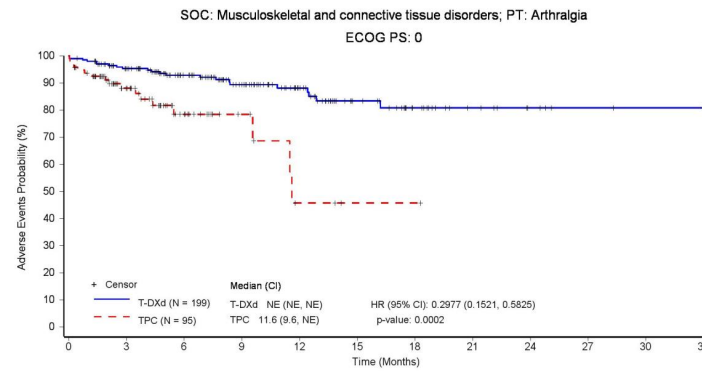
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 199)	199	170	128	93	60	36	20	10	5	2	1	0
TPC (N = 95)	95	51	21	9	3	1	1	0	0	0	0	0

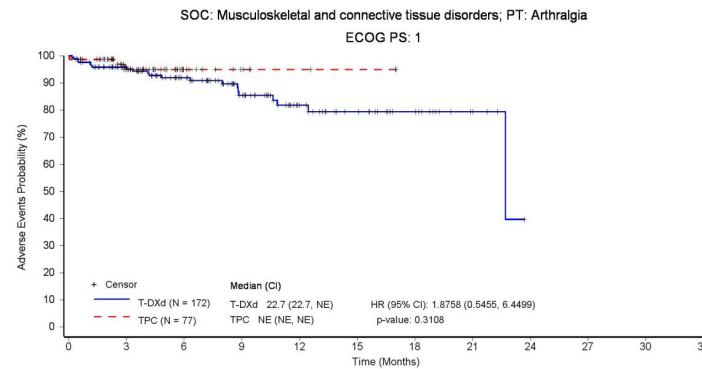
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 172)	172	130	92	60	35	23	14	4	0	0	0	0
TPC (N = 77)	77	47	14	6	3	2	0	0	0	0	0	0

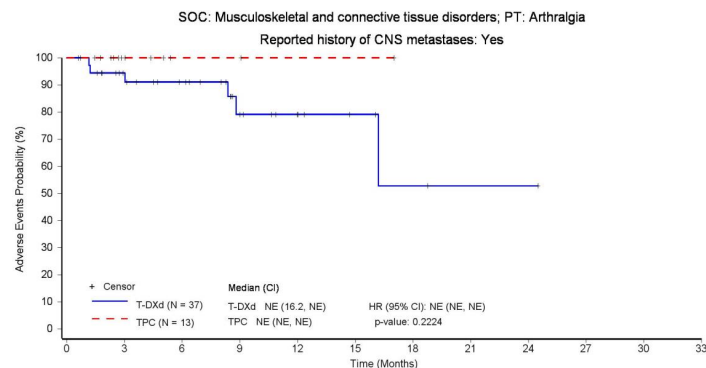
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 37)	37	28	22	12	7	4	2	1	1	0	0	0
TPC (N = 13)	13	6	2	2	1	1	0	0	0	0	0	0

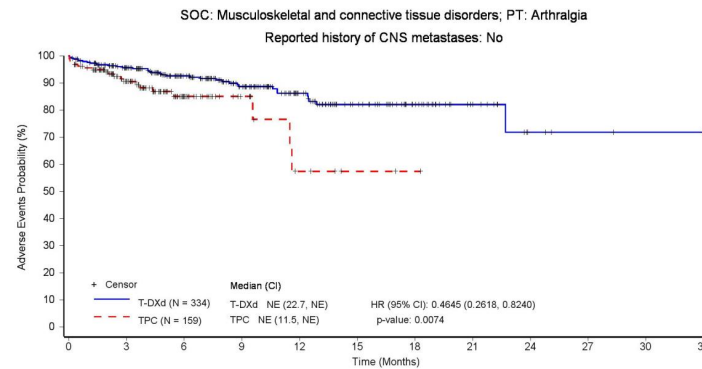
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 334)	334	272	198	141	88	55	32	13	4	2	1	0
TPC (N = 159)	159	92	33	13	5	2	1	0	0	0	0	0

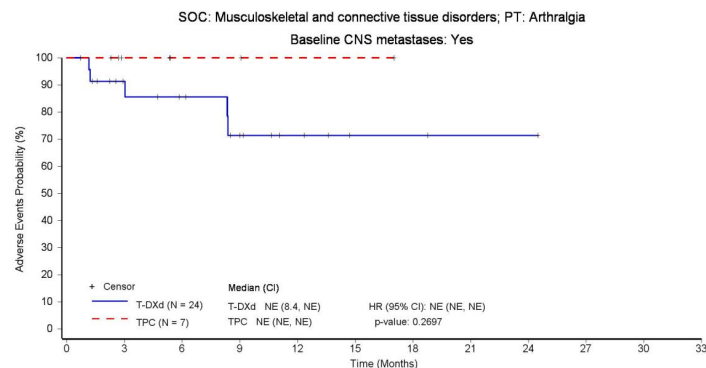
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 24)	24	16	13	9	5	2	2	1	1	0	0	0
TPC (N = 7)	7	4	2	2	1	1	0	0	0	0	0	0

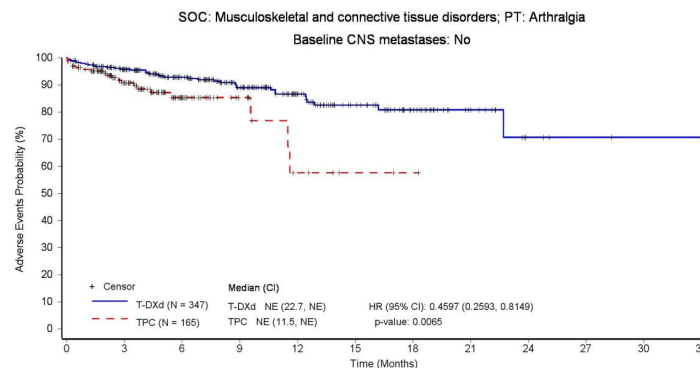
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 347)	347	284	207	144	90	57	32	13	4	2	1	0
TPC (N = 165)	165	94	33	13	5	2	1	0	0	0	0	0

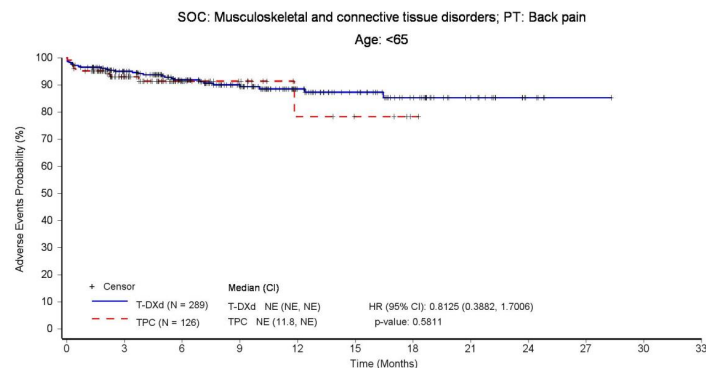
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 289)	289	235	172	127	75	53	33	16	5	1	0	0
TPC (N = 126)	126	66	28	14	6	4	1	0	0	0	0	0

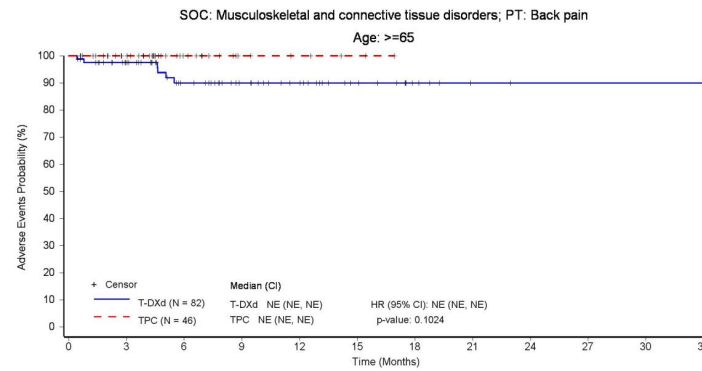
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 82)	82	63	43	30	23	14	6	2	1	1	1	0
TPC (N = 46)	46	34	15	6	4	2	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

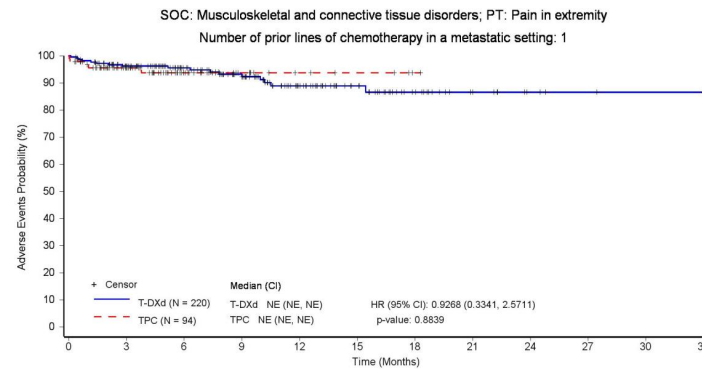
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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 220)	220	178	133	101	62	40	20	9	4	2	1	0
TPC (N = 94)	94	60	26	12	6	4	1	0	0	0	0	0

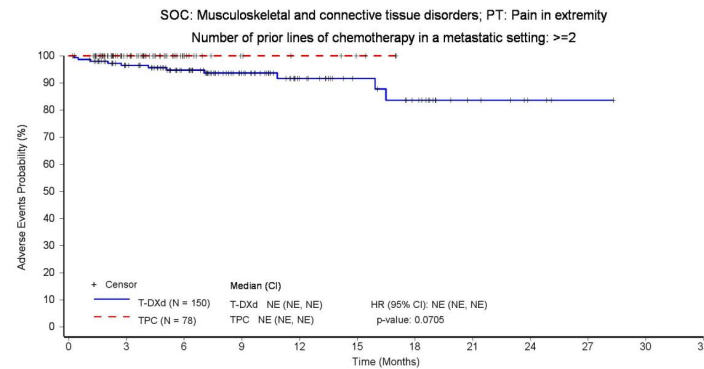
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 150)	150	123	94	62	36	24	17	7	3	1	0	0
TPC (N = 78)	78	46	16	7	5	3	0	0	0	0	0	0

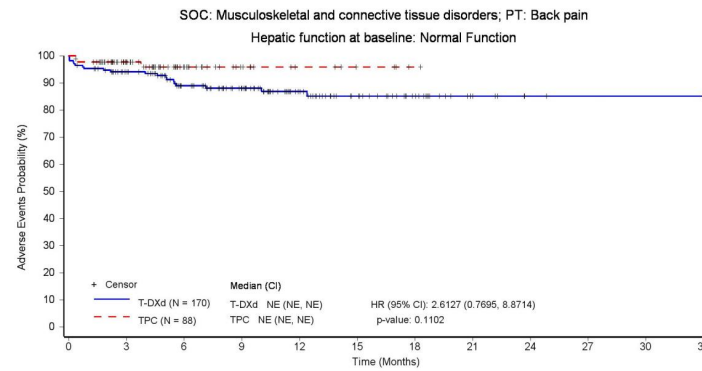
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:32; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PAT\_4\_SAS.rf

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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 170)	170	145	111	86	52	35	19	6	2	1	1	0
TPC (N = 88)	88	59	27	13	7	4	1	0	0	0	0	0

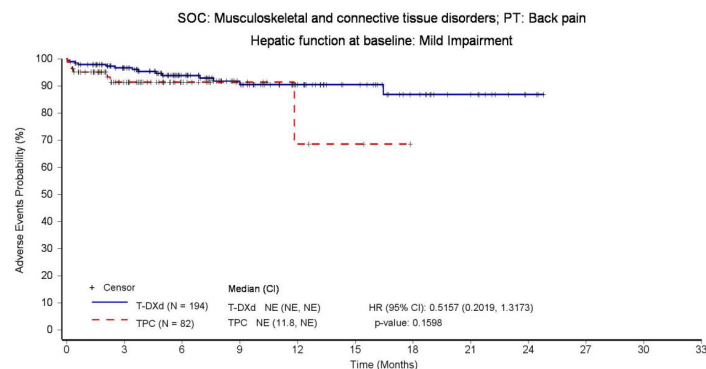
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 194)	194	150	102	69	45	31	19	11	3	0	0	0
TPC (N = 82)	82	41	16	7	3	2	0	0	0	0	0	0

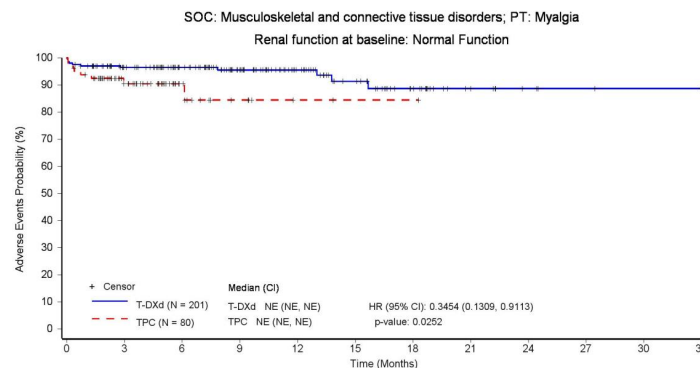
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 201)	201	166	124	90	57	38	22	8	4	2	1	0
TPC (N = 80)	80	43	16	6	2	1	1	0	0	0	0	0

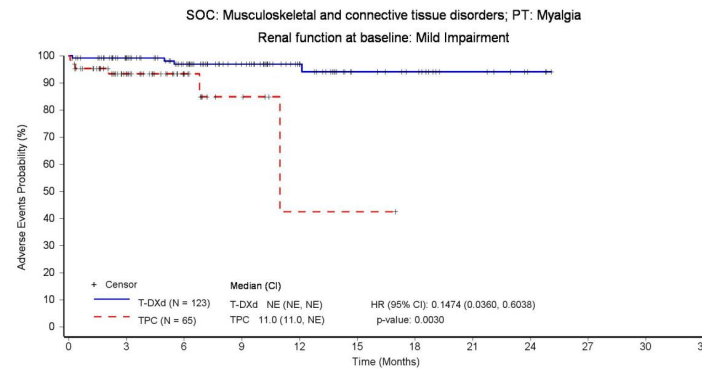
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:32; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PAT\_4\_SAS.rf

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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 123)	123	102	78	56	35	19	15	8	3	0	0	0
TPC (N = 65)	65	36	14	5	1	1	0	0	0	0	0	0

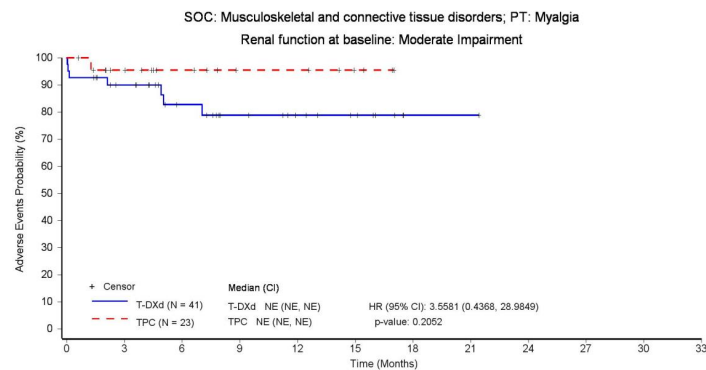
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:32; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PAT\_4\_SAS.rf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 41)	41	31	21	14	10	7	1	1	0	0	0	0
TPC (N = 23)	23	17	10	6	6	3	0	0	0	0	0	0

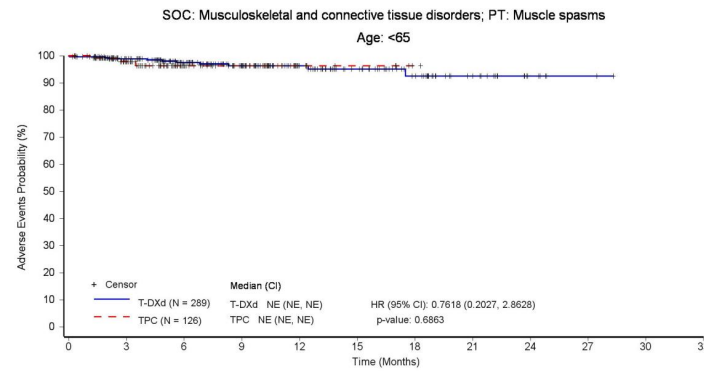
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 289)	289	247	185	135	82	55	35	17	6	2	0	0
TPC (N = 126)	126	71	28	13	6	5	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

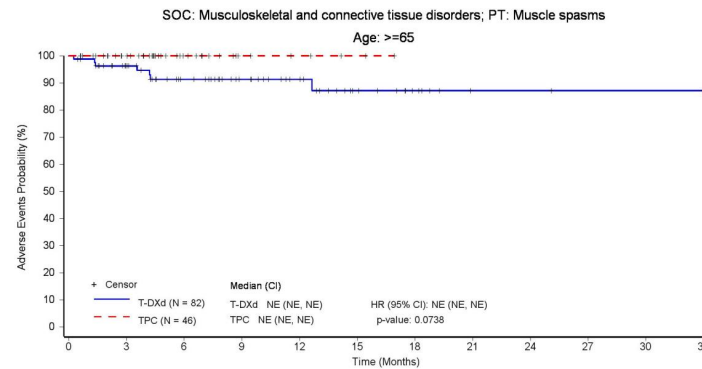
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 82)	82	62	45	32	24	14	7	2	2	1	1	0
TPC (N = 46)	46	34	15	6	4	2	0	0	0	0	0	0

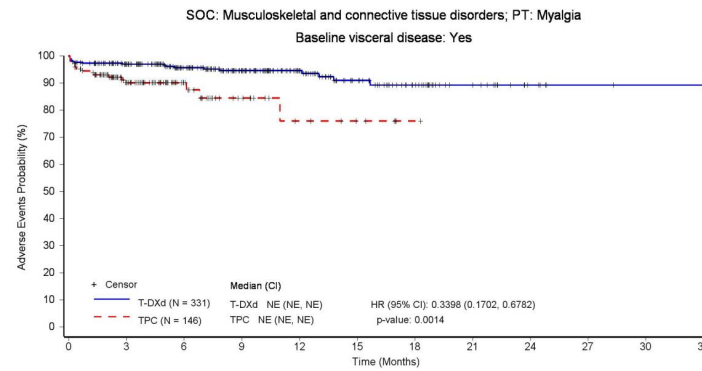
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 331)	331	268	197	141	90	57	34	16	6	2	1	0
TPC (N = 146)	146	83	35	16	8	5	1	0	0	0	0	0

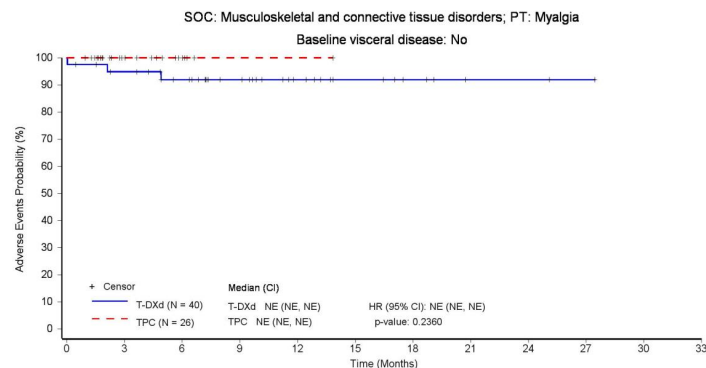
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 40)	40	35	29	21	13	8	5	2	2	1	0	0
TPC (N = 26)	26	14	5	1	1	0	0	0	0	0	0	0

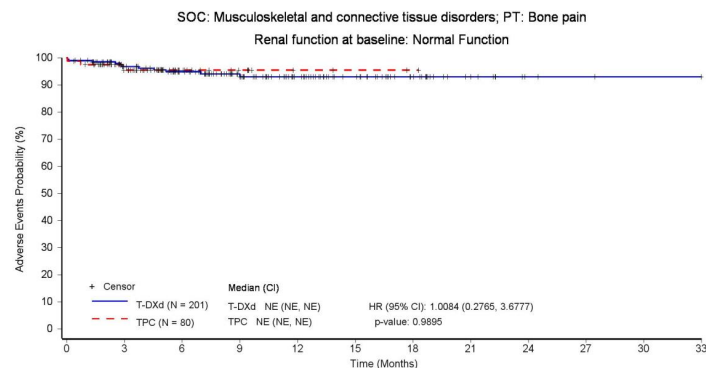
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 201)	201	166	122	88	57	39	23	9	3	2	1	0
TPC (N = 80)	80	46	17	8	3	2	1	0	0	0	0	0

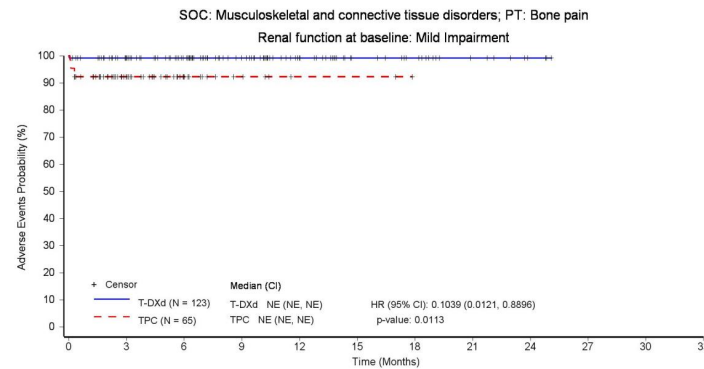
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

T-DXd (N = 123)	123	103	81	58	37	22	16	8	3	0	0	0
TPC (N = 65)	65	35	14	6	2	2	0	0	0	0	0	0

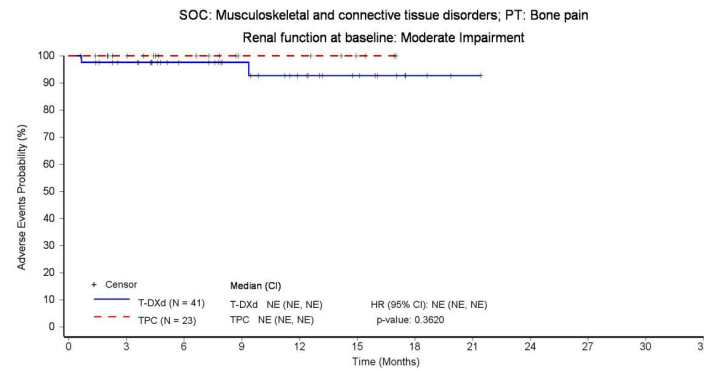
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 41)	41	35	26	20	14	9	3	1	0	0	0	0
TPC (N = 23)	23	18	11	6	6	3	0	0	0	0	0	0

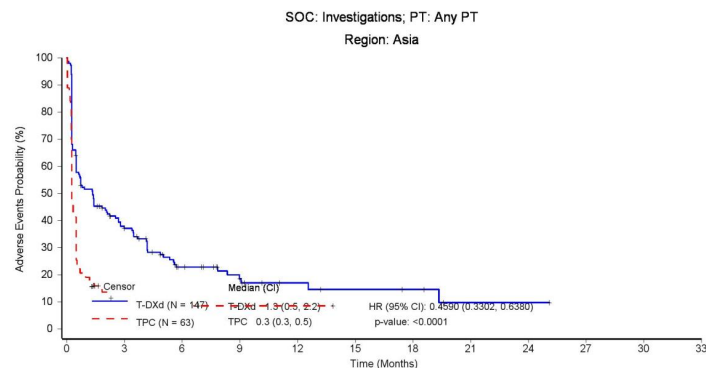
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 147)	147	48	22	13	7	5	4	1	1	0	0	0
TPC (N = 63)	63	4	3	1	1	0	0	0	0	0	0	0

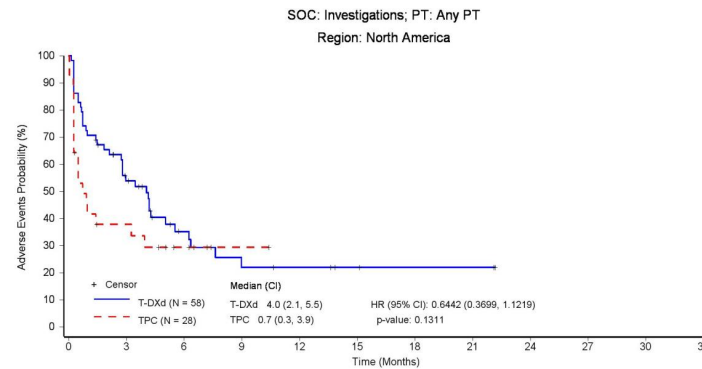
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 58)	58	27	12	6	5	3	2	2	0	0	0	0
TPC (N = 28)	28	9	3	1	0	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

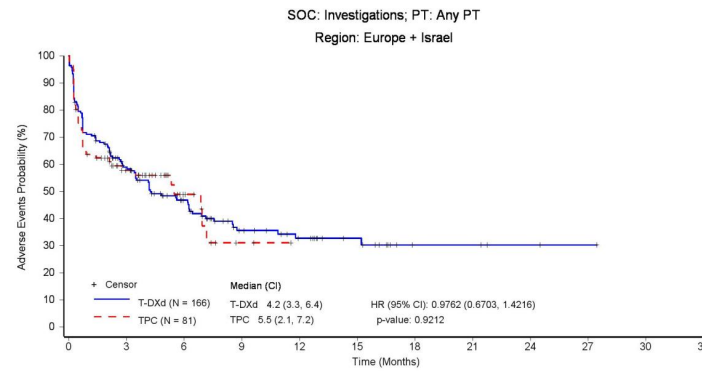
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 166)	166	86	56	30	21	13	4	4	2	1	0	0
TPC (N = 81)	81	33	11	2	0	0	0	0	0	0	0	0

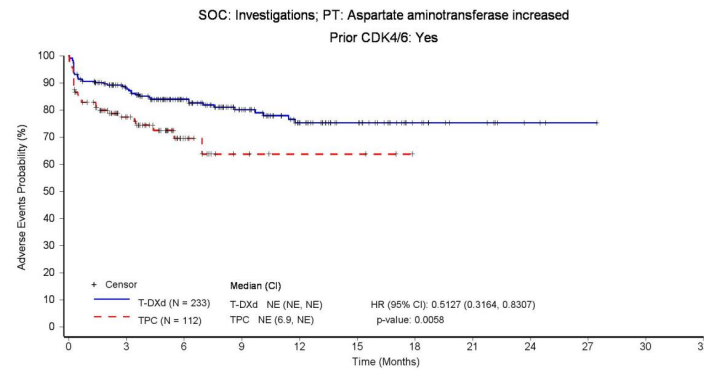
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

T-DXd (N = 233)	233	173	121	82	52	34	15	8	3	1	0	0
TPC (N = 112)	112	56	17	5	3	3	0	0	0	0	0	0

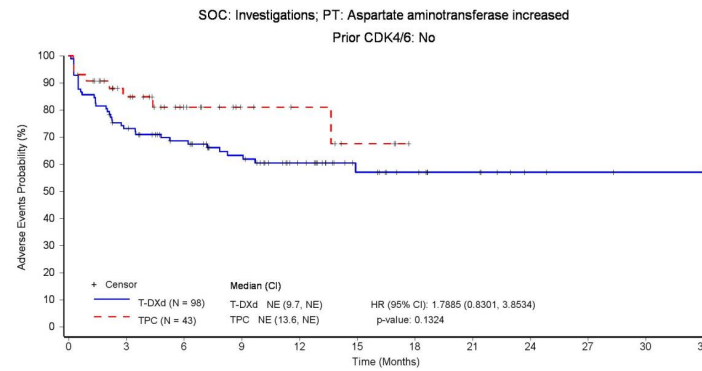
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 98)	98	69	57	45	30	17	12	8	3	2	1	0
TPC (N = 43)	43	28	15	8	6	3	0	0	0	0	0	0

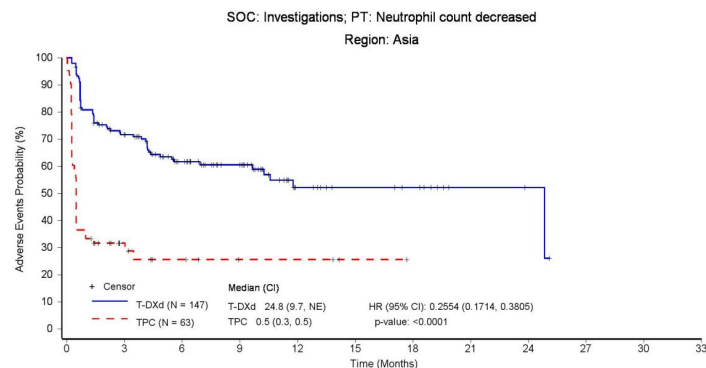
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:32; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PAT\_4\_SAS.rf

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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 147)	147	95	60	44	16	11	9	3	2	0	0	0
TPC (N = 63)	63	11	6	3	3	1	0	0	0	0	0	0

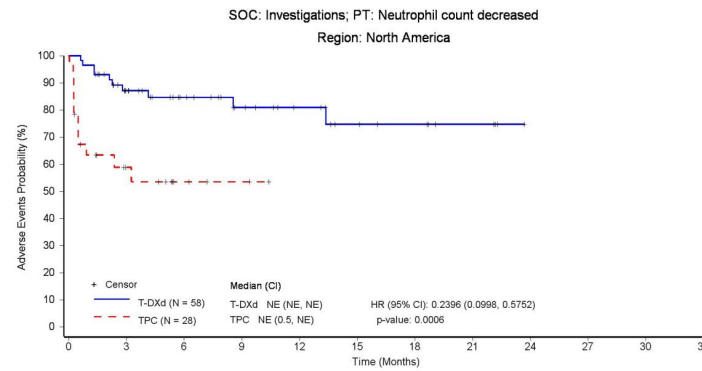
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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 Run date: 21OCT2022 – 17:32; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PAT\_4\_SAS.rf

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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

T-DXd (N = 58)	58	39	28	20	15	9	7	4	0	0	0	0
TPC (N = 28)	28	11	4	2	0	0	0	0	0	0	0	0

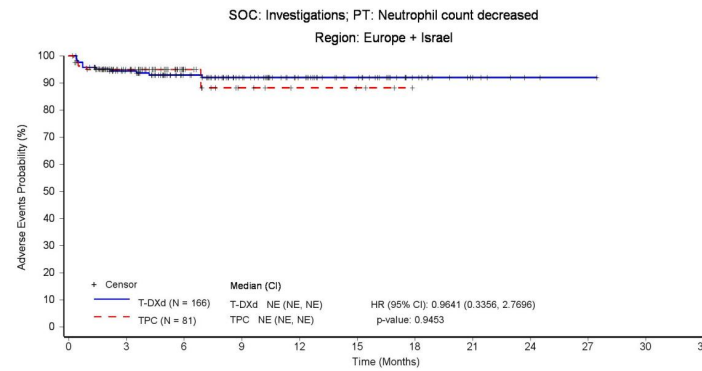
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 166)	166	132	100	71	48	34	16	6	2	1	0	0
TPC (N = 81)	81	49	17	7	4	3	0	0	0	0	0	0

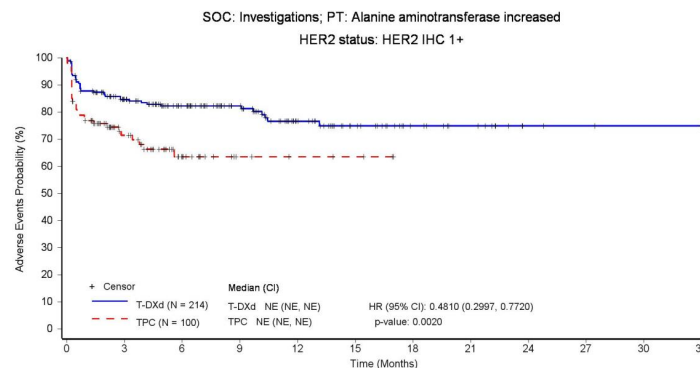
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 214)	214	150	113	85	49	29	16	11	3	2	1	0
TPC (N = 100)	100	46	20	6	4	3	0	0	0	0	0	0

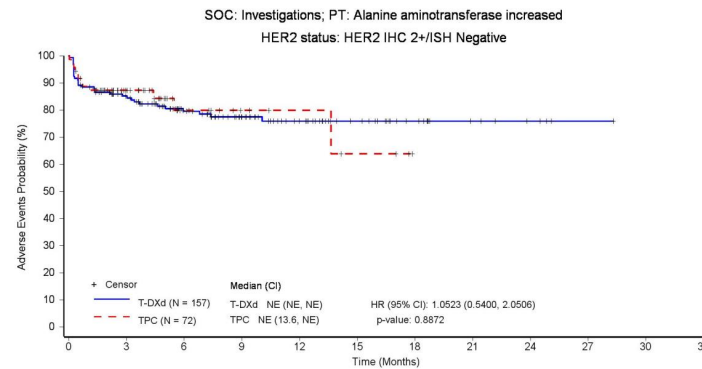
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

T-DXd (N = 157)	157	117	81	57	38	24	14	7	4	1	0	0
TPC (N = 72)	72	40	13	7	5	3	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

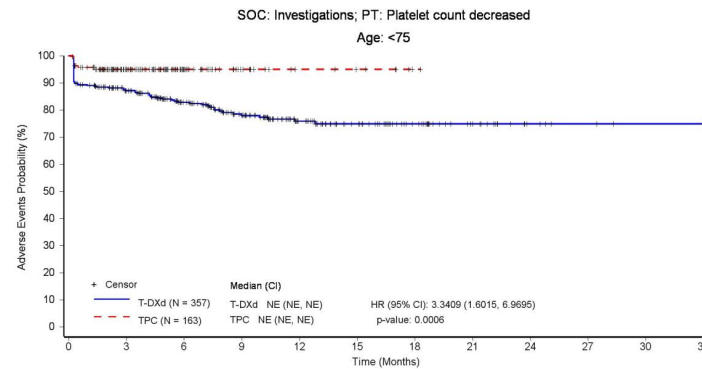
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 357)	357	265	194	141	88	60	35	17	6	3	1	0
TPC (N = 163)	163	97	39	17	8	6	1	0	0	0	0	0

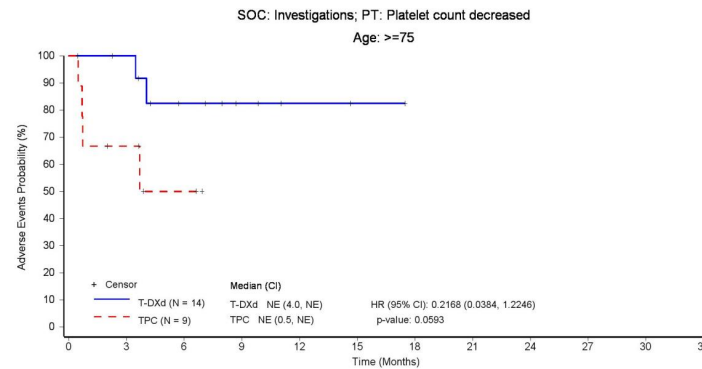
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 14)	14	12	7	4	2	1	0	0	0	0	0	0
TPC (N = 9)	9	5	2	0	0	0	0	0	0	0	0	0

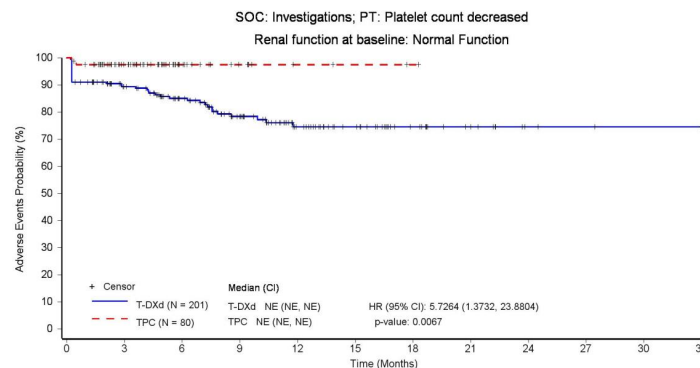
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 201)	201	155	113	80	47	33	18	9	3	2	1	0
TPC (N = 80)	80	49	18	8	3	2	1	0	0	0	0	0

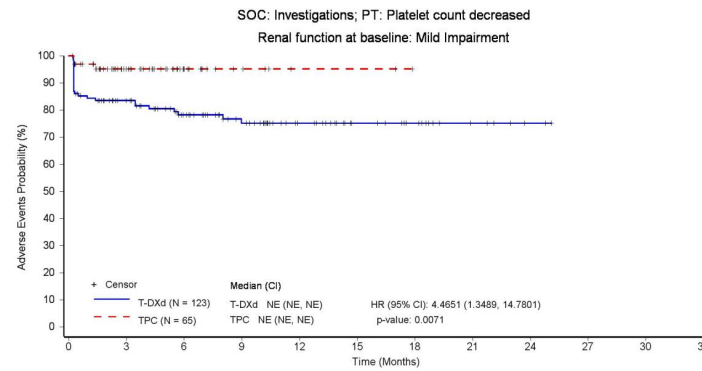
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 123)	123	86	64	47	30	19	13	6	2	0	0	0
TPC (N = 65)	65	37	15	6	2	2	0	0	0	0	0	0

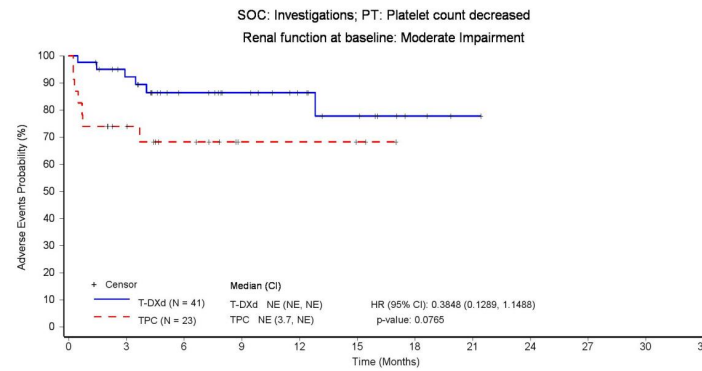
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 41)	41	33	22	17	12	8	3	1	0	0	0	0
TPC (N = 23)	23	14	8	3	3	2	0	0	0	0	0	0

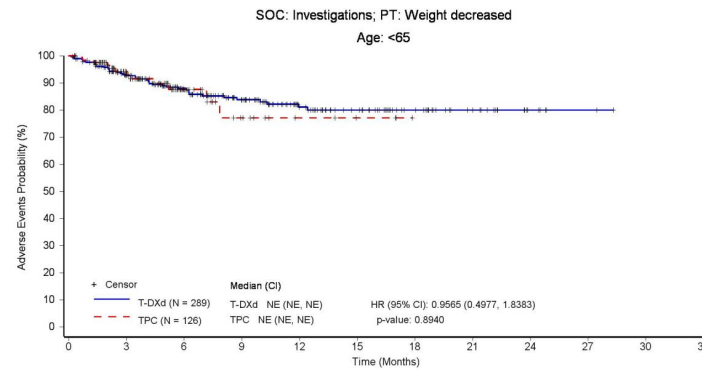
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 289)	289	231	168	118	74	52	33	17	6	2	0	0
TPC (N = 126)	126	70	27	11	5	3	0	0	0	0	0	0

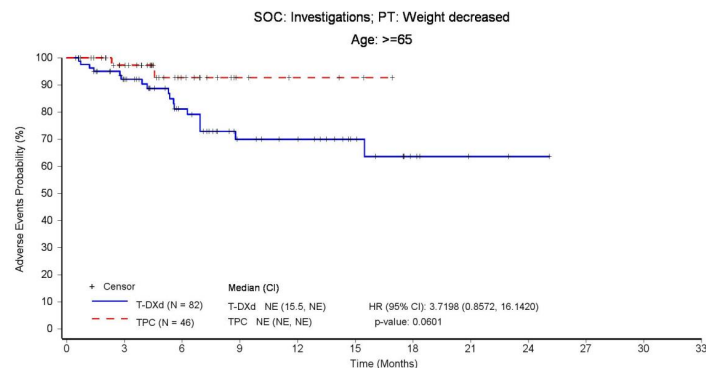
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 82)	82	60	40	23	20	12	5	2	1	0	0	0
TPC (N = 46)	46	33	14	5	3	2	0	0	0	0	0	0

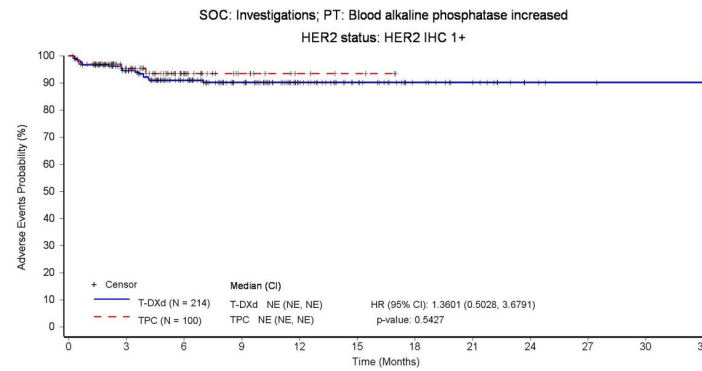
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 214)	214	168	125	93	57	36	20	12	4	2	1	0
TPC (N = 100)	100	58	27	11	5	3	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

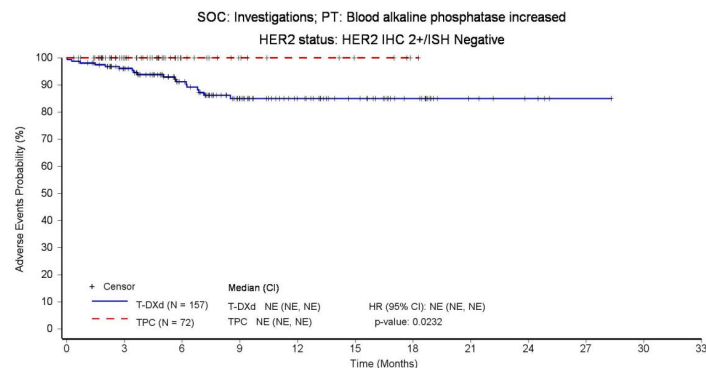
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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 157)	157	132	94	63	43	30	18	7	4	1	0	0
TPC (N = 72)	72	47	17	9	6	4	1	0	0	0	0	0

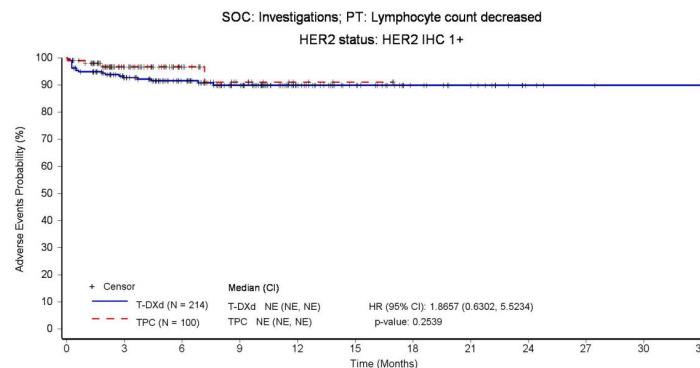
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 214)	214	165	126	94	57	36	20	13	4	2	1	0
TPC (N = 100)	100	57	25	10	4	2	0	0	0	0	0	0

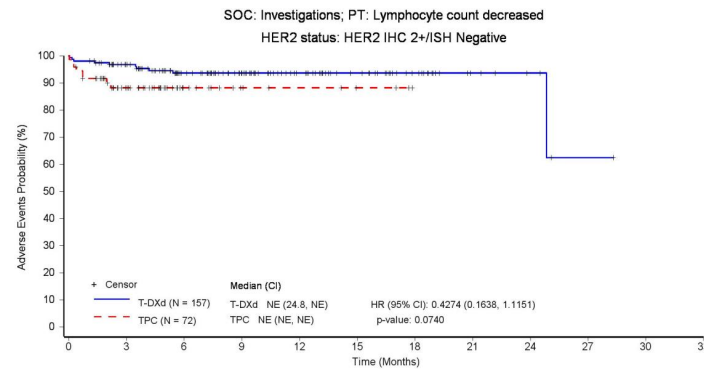
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 157)	157	133	96	71	47	32	19	7	4	1	0	0
TPC (N = 72)	72	43	15	7	5	3	0	0	0	0	0	0

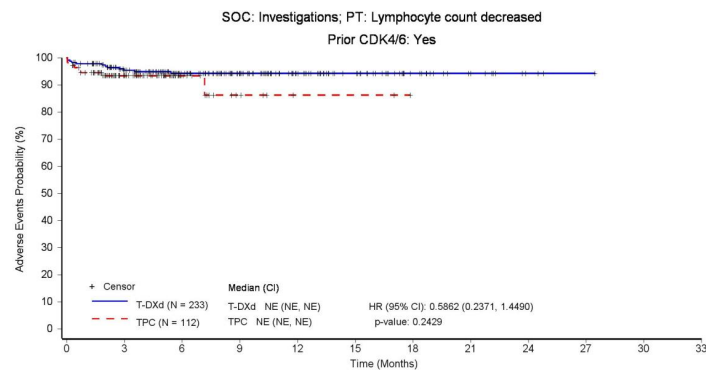
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 233)	233	184	134	95	62	42	20	9	3	1	0	0
TPC (N = 112)	112	61	19	6	2	2	0	0	0	0	0	0

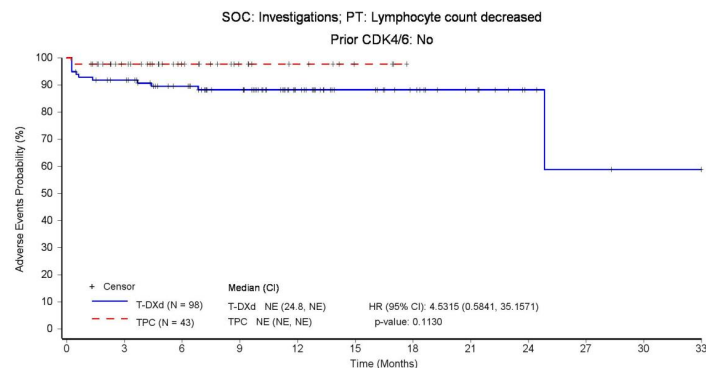
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 98)	98	86	71	60	35	22	16	10	4	2	1	0
TPC (N = 43)	43	32	19	11	7	3	0	0	0	0	0	0

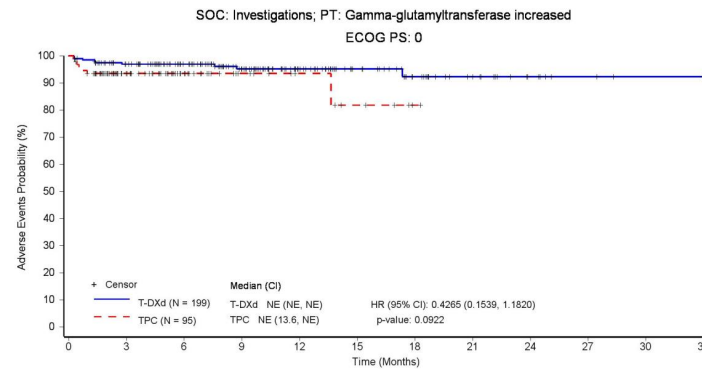
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

T-DXd (N = 199)	199	173	137	102	66	44	27	15	7	3	1	0
TPC (N = 95)	95	53	28	13	8	5	1	0	0	0	0	0

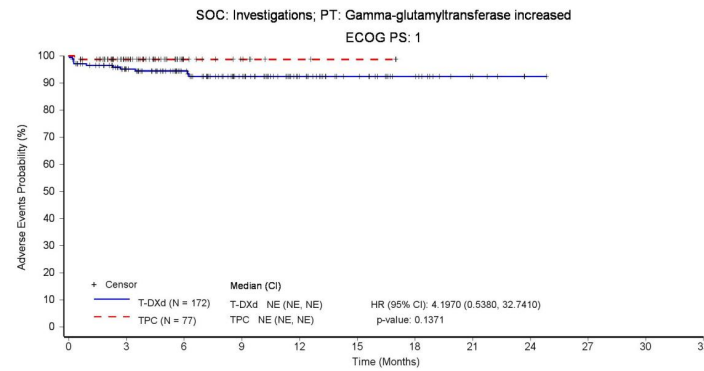
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 172)	172	131	96	66	41	26	15	5	1	0	0	0
TPC (N = 77)	77	48	14	7	3	2	0	0	0	0	0	0

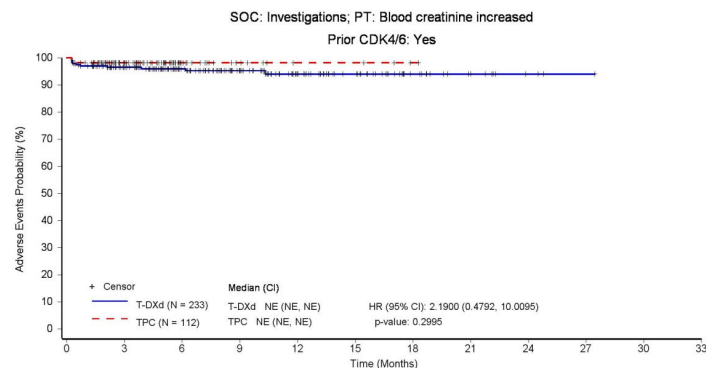
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 233)	233	186	133	92	60	41	19	8	3	1	0	0
TPC (N = 112)	112	66	22	9	4	4	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

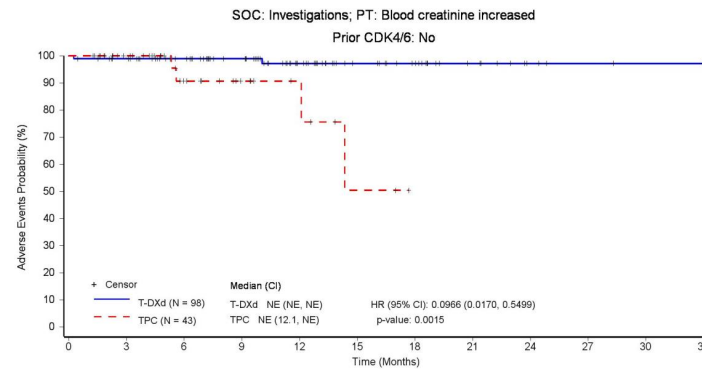
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 98)	98	92	78	65	40	25	19	10	4	2	1	0
TPC (N = 43)	43	32	17	10	6	2	0	0	0	0	0	0

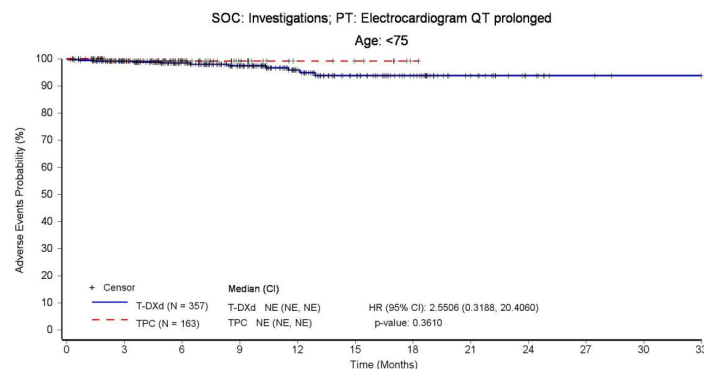
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 357)	357	300	226	165	103	67	41	19	8	3	1	0
TPC (N = 163)	163	98	39	17	8	6	1	0	0	0	0	0

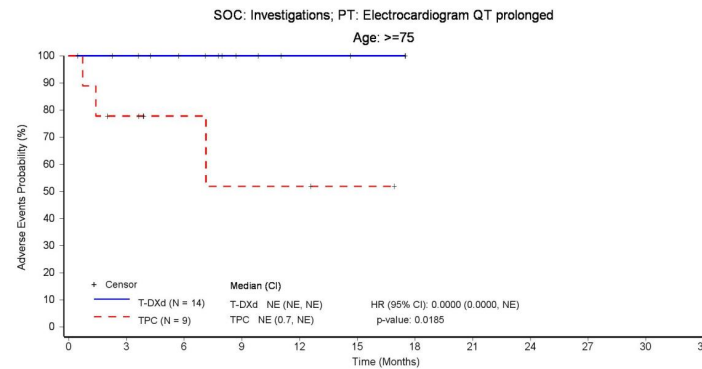
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 14)	14	12	9	5	3	2	0	0	0	0	0	0
TPC (N = 9)	9	6	3	2	2	1	0	0	0	0	0	0

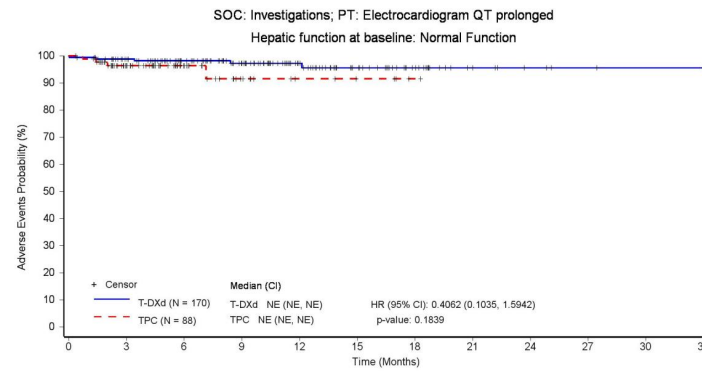
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 170)	170	153	124	96	60	38	20	7	4	2	1	0
TPC (N = 88)	88	58	26	12	6	4	1	0	0	0	0	0

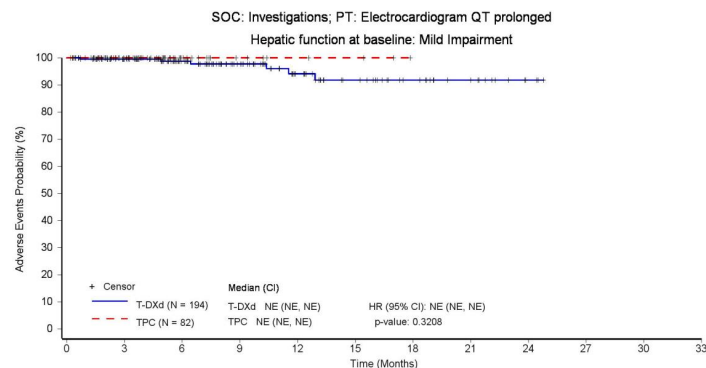
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 194)	194	156	109	72	45	30	20	11	3	0	0	0
TPC (N = 82)	82	46	16	7	4	3	0	0	0	0	0	0

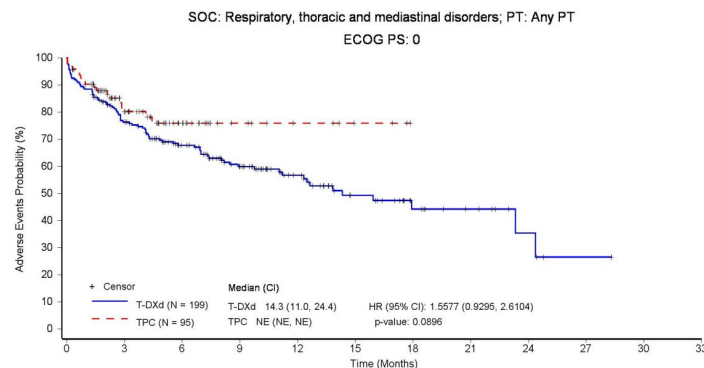
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 199)	199	141	104	75	45	26	14	9	4	1	0	0
TPC (N = 95)	95	48	23	10	6	3	0	0	0	0	0	0

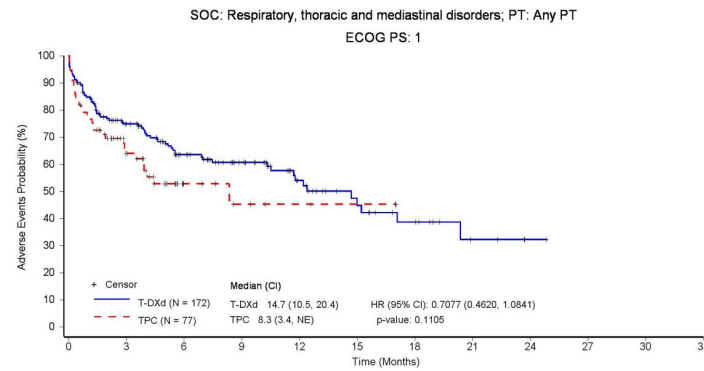
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 172)	172	109	72	50	28	17	11	4	1	0	0	0
TPC (N = 77)	77	33	10	5	3	2	0	0	0	0	0	0

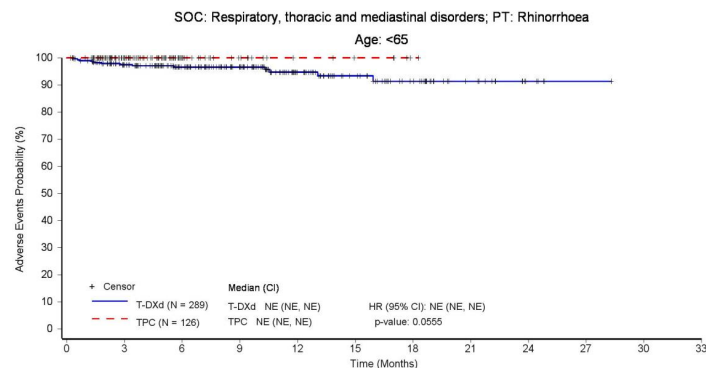
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 289)	289	242	182	135	77	51	32	15	5	1	0	0
TPC (N = 126)	126	73	29	14	7	5	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

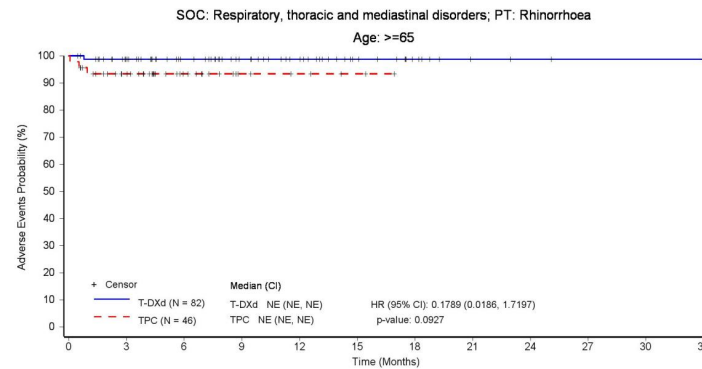
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 82)	82	64	49	35	27	16	8	3	2	1	1	0
TPC (N = 46)	46	32	15	6	4	2	0	0	0	0	0	0

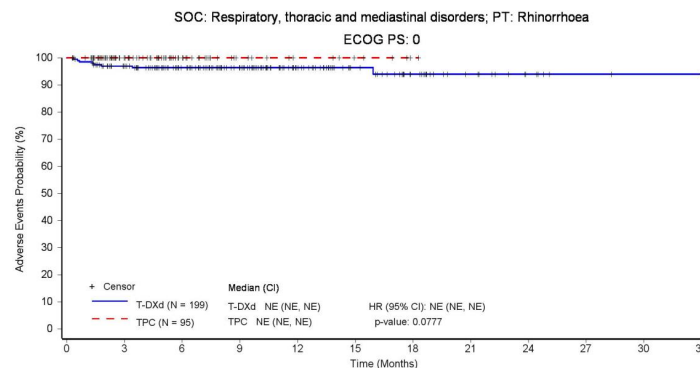
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 199)	199	172	133	102	63	41	25	13	6	2	1	0
TPC (N = 95)	95	58	29	13	8	5	1	0	0	0	0	0

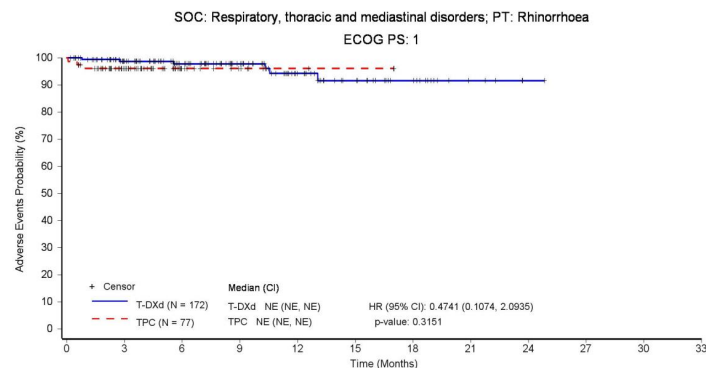
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 172)	172	134	98	68	41	26	15	5	1	0	0	0
TPC (N = 77)	77	47	15	7	3	2	0	0	0	0	0	0

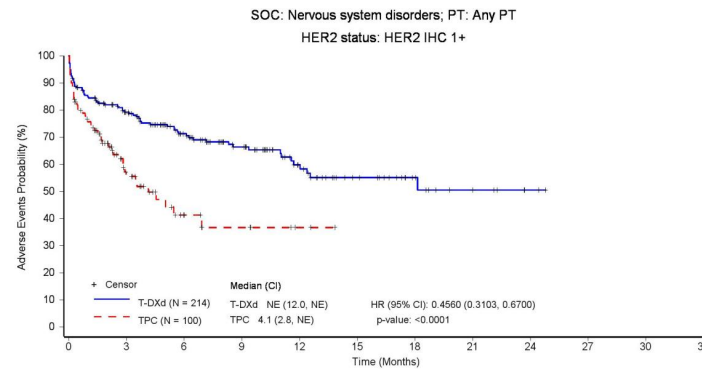
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 214)	214	142	99	69	39	23	13	6	2	0	0	0
TPC (N = 100)	100	33	11	6	2	0	0	0	0	0	0	0

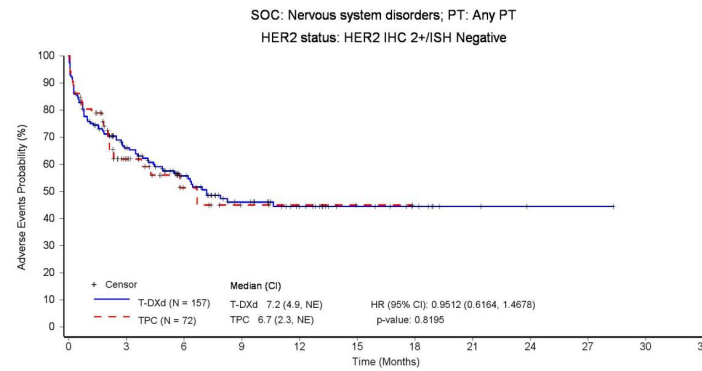
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 157)	157	89	56	35	21	12	8	3	1	1	0	0
TPC (N = 72)	72	28	9	3	2	1	0	0	0	0	0	0

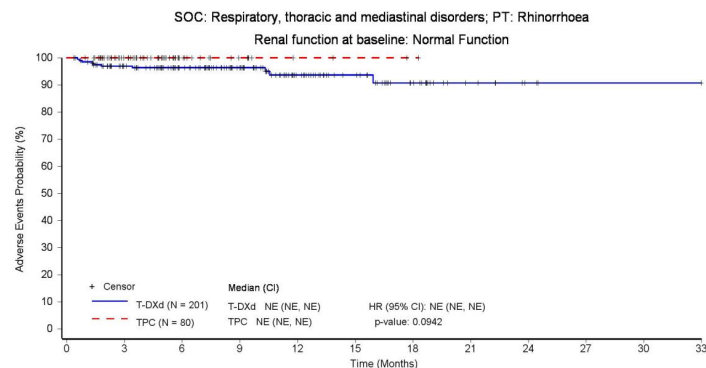
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 201)	201	166	123	91	53	36	20	8	3	1	1	0
TPC (N = 80)	80	49	18	8	3	2	1	0	0	0	0	0

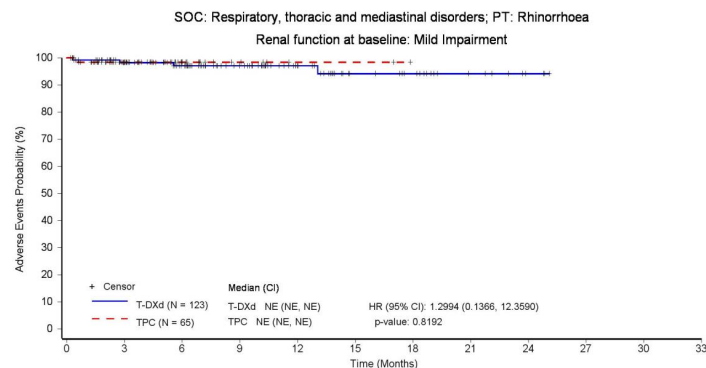
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:32; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PAT\_4\_SAS.rf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 123)	123	101	79	57	36	21	16	8	3	0	0	0
TPC (N = 65)	65	37	15	6	2	2	0	0	0	0	0	0

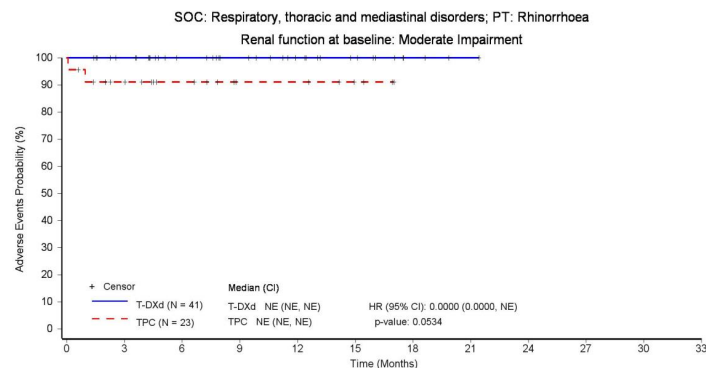
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 41)	41	35	26	20	14	9	3	1	0	0	0	0
TPC (N = 23)	23	17	11	6	6	3	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

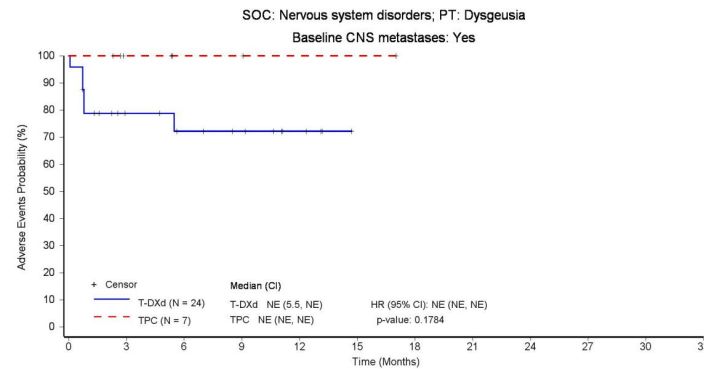
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 24)	24	13	10	8	4	0	0	0	0	0	0	0
TPC (N = 7)	7	4	2	2	1	1	0	0	0	0	0	0

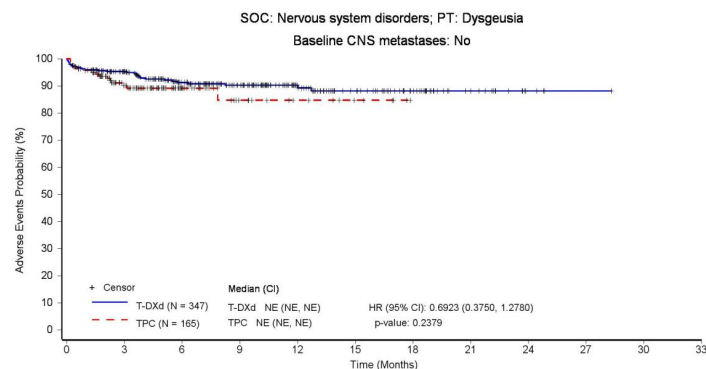
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Patients still at risk:

Time (Months)	T-DXd (N = 347)	TPC (N = 165)
0	347	165
3	282	93
6	204	36
9	147	15
12	90	9
15	60	5
18	37	0
21	15	0
24	4	0
27	1	0
30	0	0
33	0	0

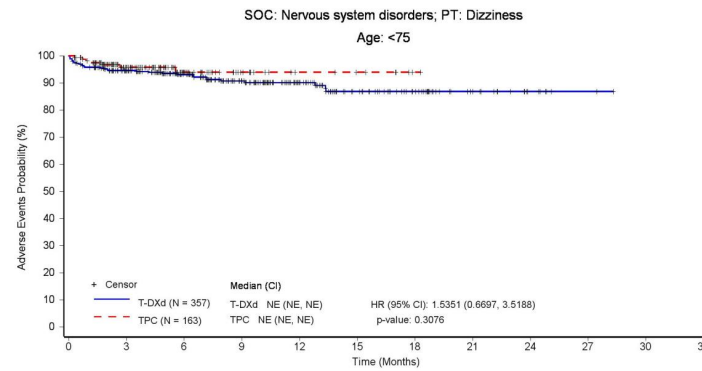
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 357)	357	286	214	154	98	61	39	17	7	2	0	0
TPC (N = 163)	163	95	38	17	8	6	1	0	0	0	0	0

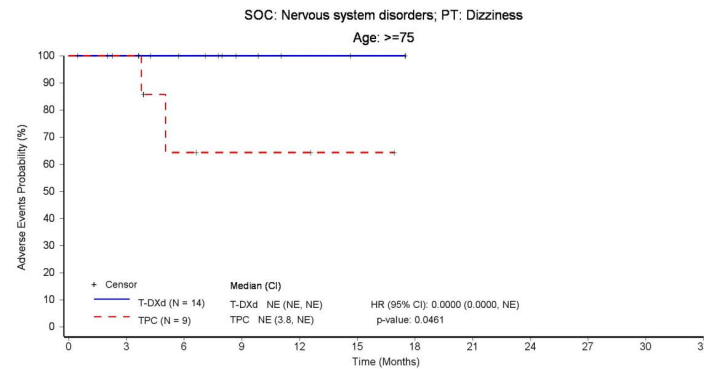
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 14)	14	12	9	5	3	2	0	0	0	0	0	0
TPC (N = 9)	9	8	3	2	2	1	0	0	0	0	0	0

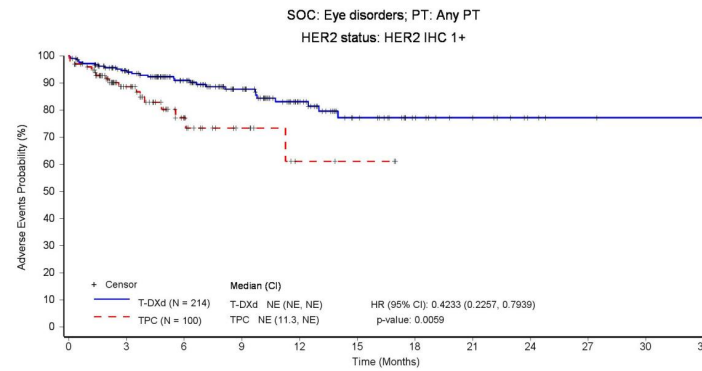
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 214)	214	168	127	90	53	28	16	9	4	2	1	0
TPC (N = 100)	100	53	22	9	3	2	0	0	0	0	0	0

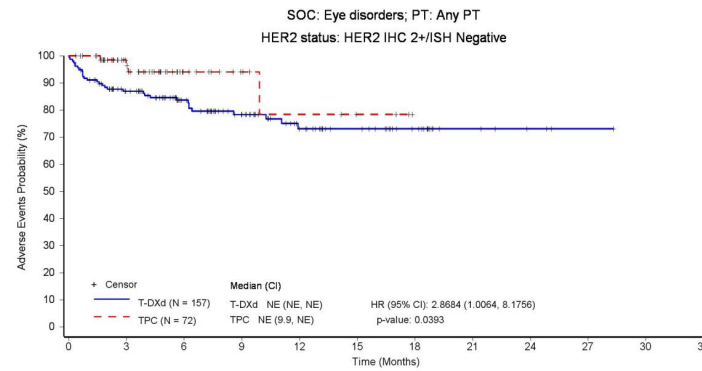
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 157)	157	117	84	59	36	26	16	6	3	1	0	0
TPC (N = 72)	72	45	16	8	5	3	0	0	0	0	0	0

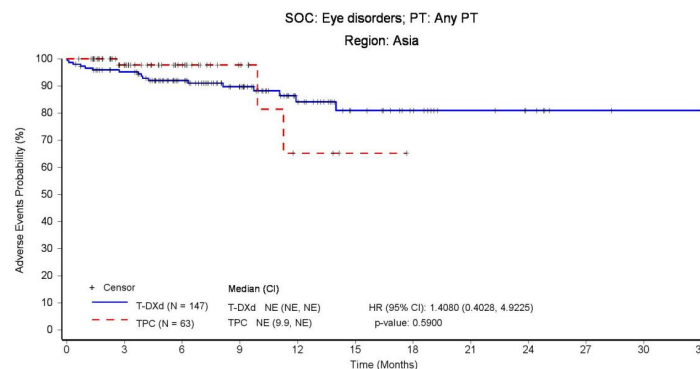
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 147)	147	127	93	68	37	22	15	9	6	2	1	0
TPC (N = 63)	63	39	20	9	3	1	0	0	0	0	0	0

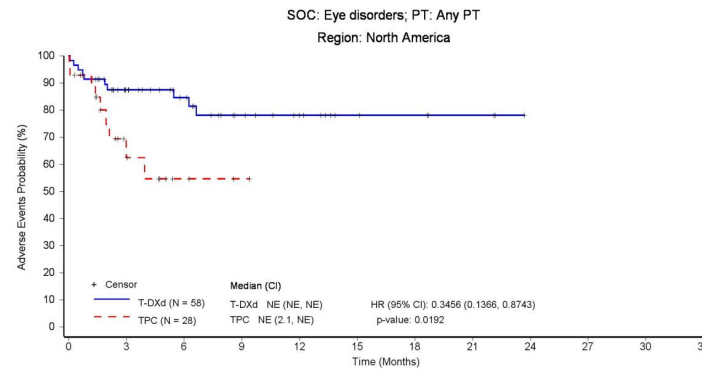
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 58)	58	38	28	18	12	6	5	3	0	0	0	0
TPC (N = 28)	28	9	3	1	0	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

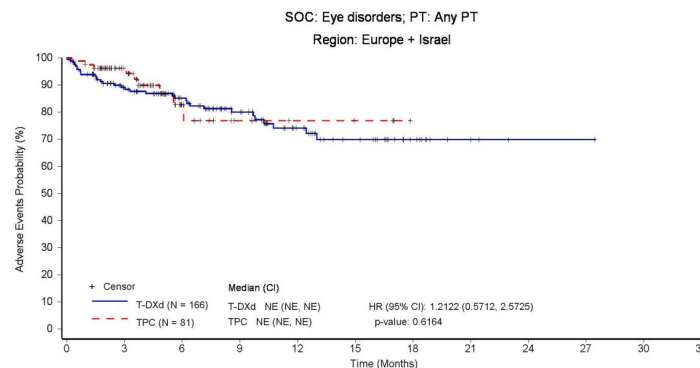
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Patients still at risk:

Time (Months)	T-DXd (N = 166)	TPC (N = 81)
0	166	81
3	120	50
6	90	15
9	63	7
12	40	5
15	26	4
18	12	0
21	3	0
24	1	0
27	1	0
30	0	0
33	0	0

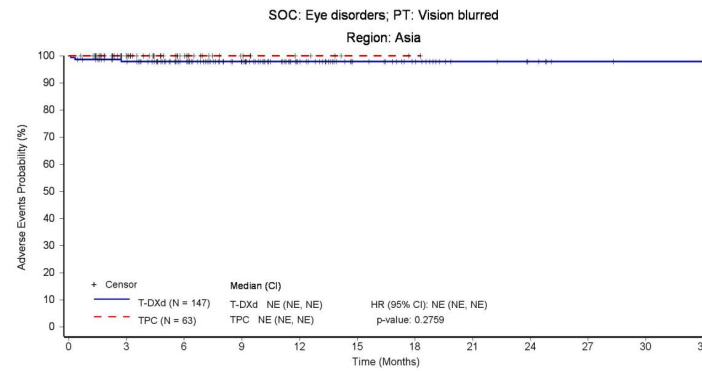
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 147)	147	130	98	74	43	26	18	9	6	2	1	0
TPC (N = 63)	63	40	20	9	5	2	1	0	0	0	0	0

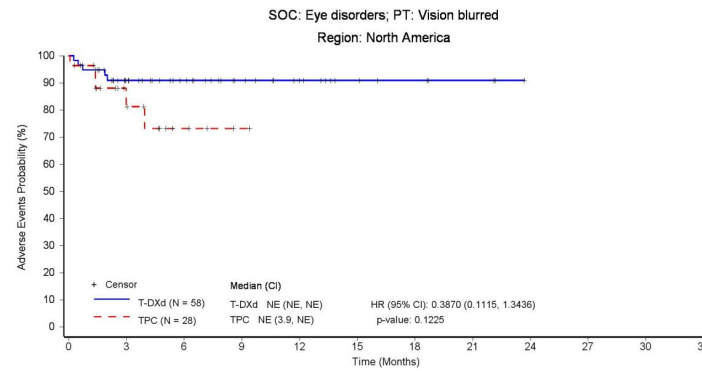
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 58)	58	40	30	21	14	8	5	3	0	0	0	0
TPC (N = 28)	28	12	4	1	0	0	0	0	0	0	0	0

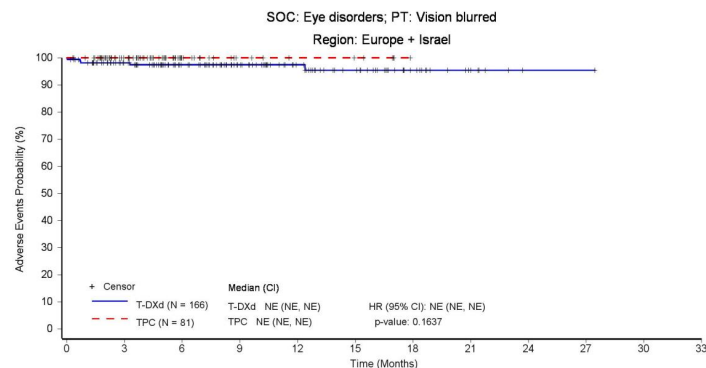
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:32; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PAT\_4\_SAS.rf

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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	T-DXd (N = 166)	TPC (N = 81)
0	166	81
3	134	52
6	101	19
9	73	9
12	50	6
15	35	5
18	17	0
21	6	0
24	1	0
27	1	0
30	0	0
33	0	0

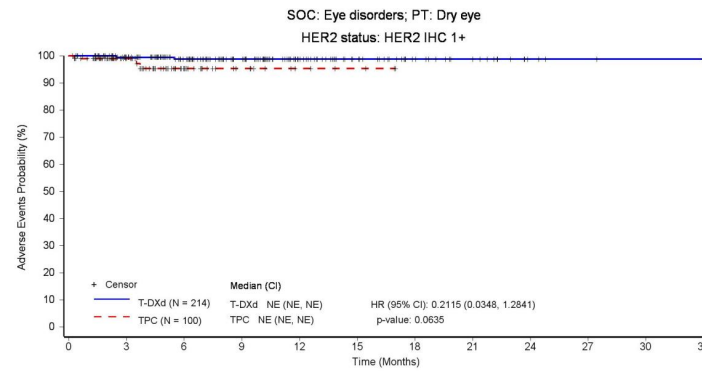
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 214)	214	177	137	100	62	39	23	13	4	2	1	0
TPC (N = 100)	100	59	25	11	5	3	0	0	0	0	0	0

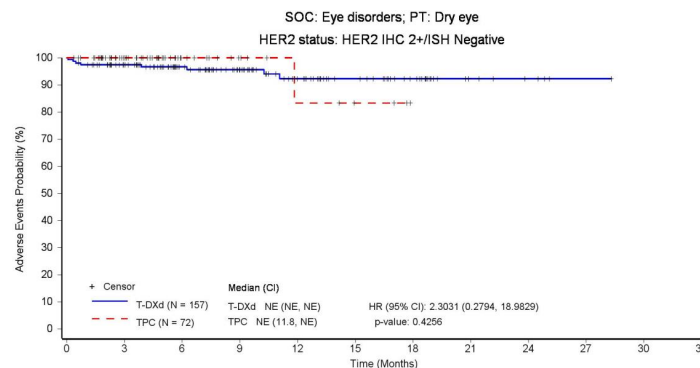
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 157)	157	132	97	71	46	32	21	7	4	1	0	0
TPC (N = 72)	72	47	17	9	5	3	0	0	0	0	0	0

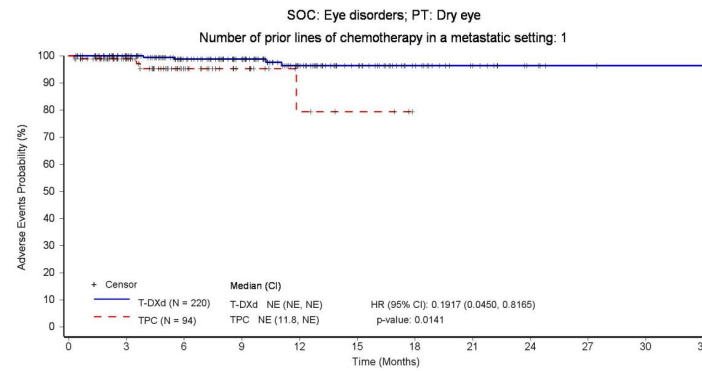
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:32; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PAT\_4\_SAS.rf

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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 220)	220	186	137	106	67	44	23	12	5	2	1	0
TPC (N = 94)	94	60	26	13	5	3	0	0	0	0	0	0

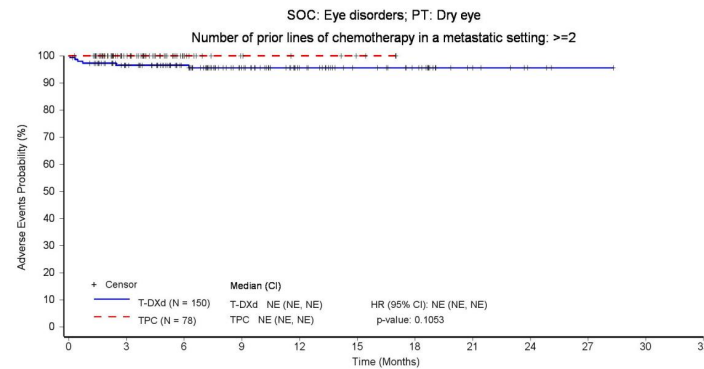
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 150)	150	122	96	64	40	26	20	7	3	1	0	0
TPC (N = 78)	78	46	16	7	5	3	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

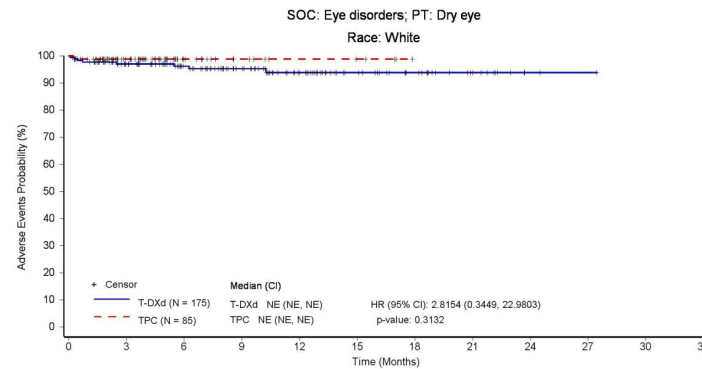
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 175)	175	137	106	79	52	33	21	10	2	1	0	0
TPC (N = 85)	85	49	18	9	5	4	0	0	0	0	0	0

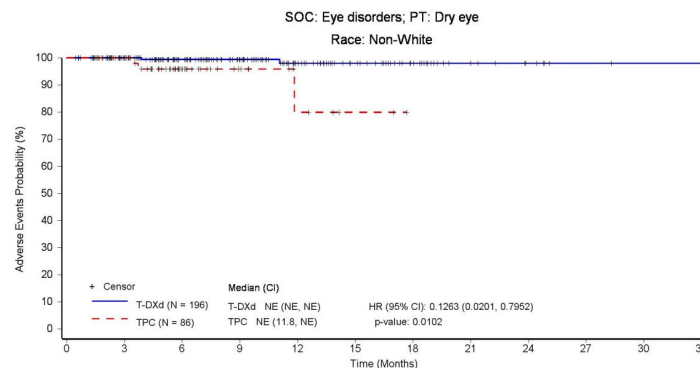
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 196)	196	172	128	92	56	38	23	10	6	2	1	0
TPC (N = 86)	86	56	24	11	5	2	0	0	0	0	0	0

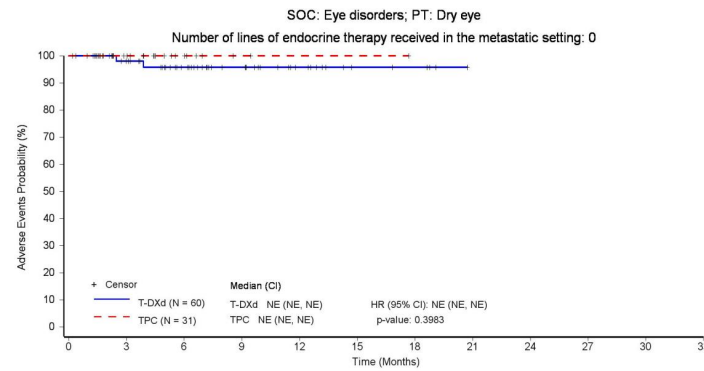
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 60)	60	48	33	22	12	5	4	0	0	0	0	0
TPC (N = 31)	31	18	7	2	1	1	0	0	0	0	0	0

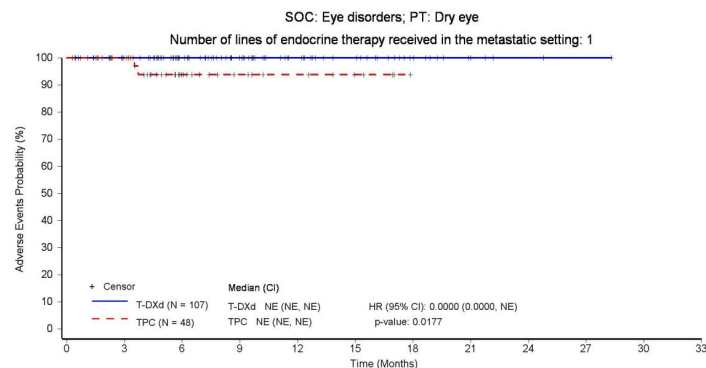
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 107)	107	91	67	47	31	22	11	4	2	1	0	0
TPC (N = 48)	48	36	17	10	7	4	0	0	0	0	0	0

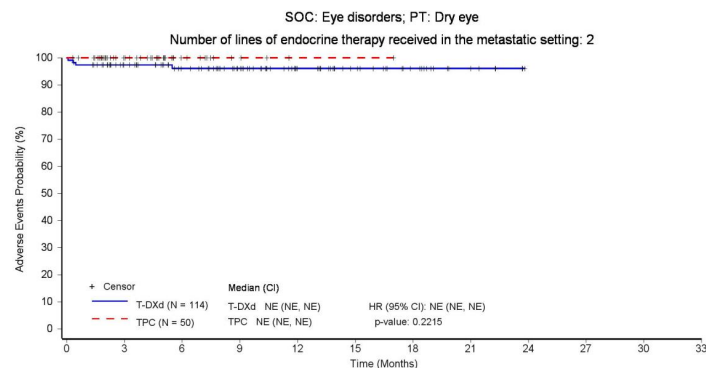
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 114)	114	90	74	58	38	25	15	6	0	0	0	0
TPC (N = 50)	50	30	11	4	1	1	0	0	0	0	0	0

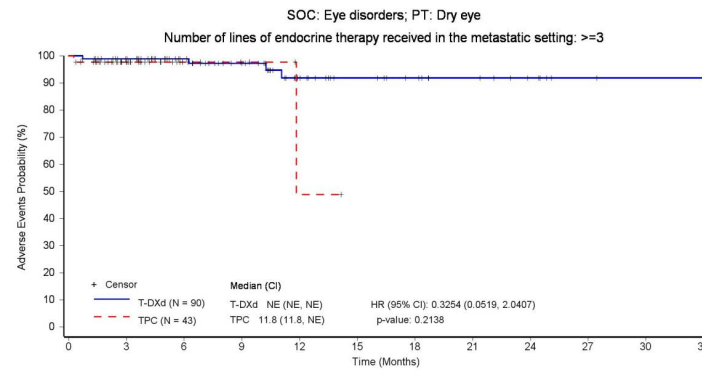
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:32; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PAT\_4\_SAS.rf

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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 90)	90	80	60	44	27	19	14	10	6	2	1	0
TPC (N = 43)	43	22	7	4	1	0	0	0	0	0	0	0

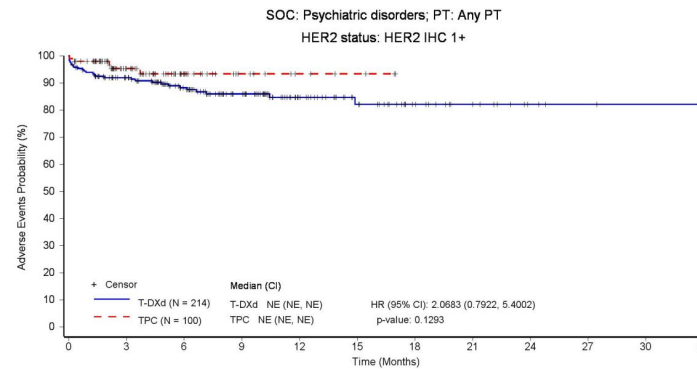
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

Time (Months)	T-DXd (N = 214)	TPC (N = 100)
0	214	100
3	166	56
6	122	25
9	88	10
12	51	5
15	32	3
18	18	0
21	10	0
24	4	0
27	2	0
30	1	0
33	0	0

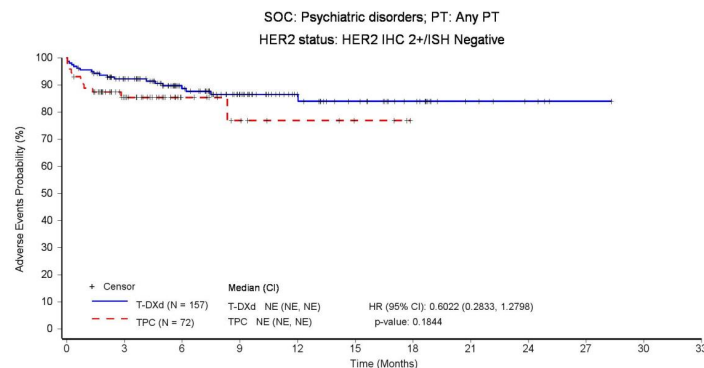
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 157)	157	126	87	59	35	26	17	7	4	1	0	0
TPC (N = 72)	72	40	14	8	5	3	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

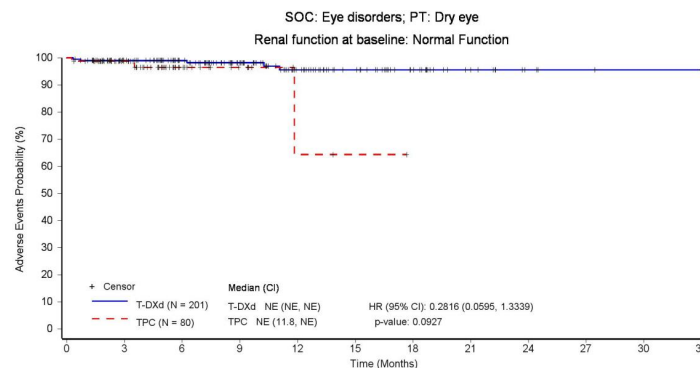
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 Run date: 21OCT2022 – 17:32; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PAT\_4\_SAS.rf



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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 201)	201	170	127	94	58	40	24	10	4	2	1	0
TPC (N = 80)	80	48	17	8	2	1	0	0	0	0	0	0

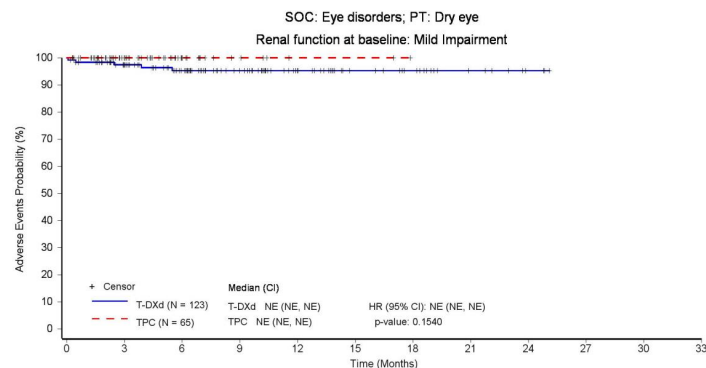
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 123)	123	100	78	55	35	21	16	8	3	0	0	0
TPC (N = 65)	65	38	15	6	2	2	0	0	0	0	0	0

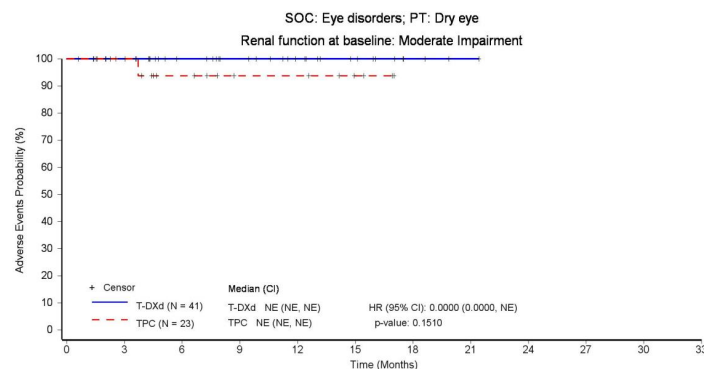
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 41)	41	35	26	20	14	9	3	1	0	0	0	0
TPC (N = 23)	23	18	10	6	6	3	0	0	0	0	0	0

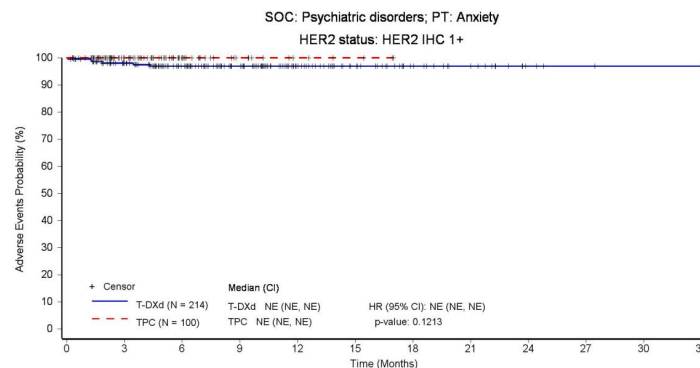
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 214)	214	175	133	98	59	38	23	13	4	2	1	0
TPC (N = 100)	100	60	27	11	5	3	0	0	0	0	0	0

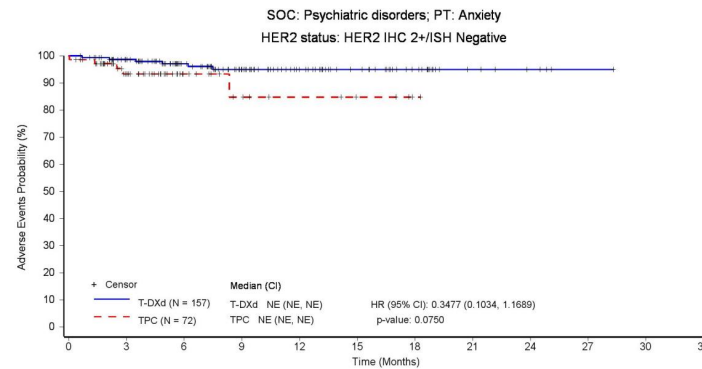
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:32; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PAT\_4\_SAS.rf

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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 157)	157	134	96	68	44	30	18	7	4	1	0	0
TPC (N = 72)	72	44	16	9	6	4	1	0	0	0	0	0

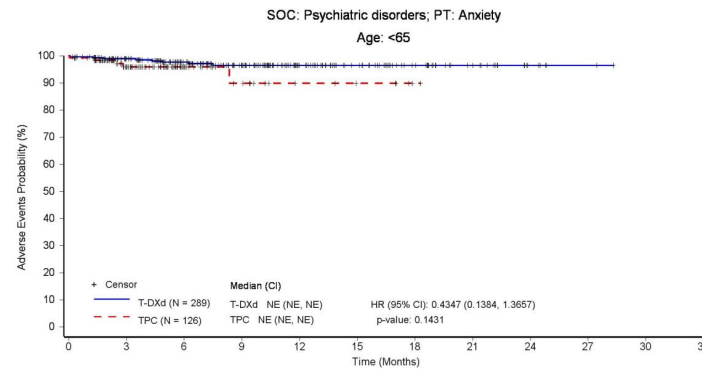
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 289)	289	246	183	134	79	54	34	17	6	2	0	0
TPC (N = 126)	126	70	28	14	7	5	1	0	0	0	0	0

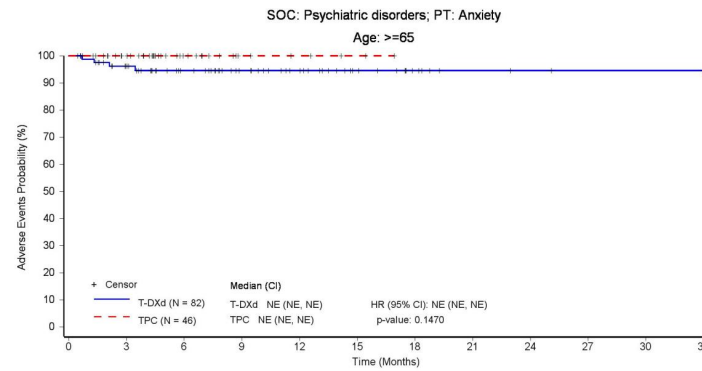
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 82)	82	63	46	32	24	14	7	3	2	1	1	0
TPC (N = 46)	46	34	15	6	4	2	0	0	0	0	0	0

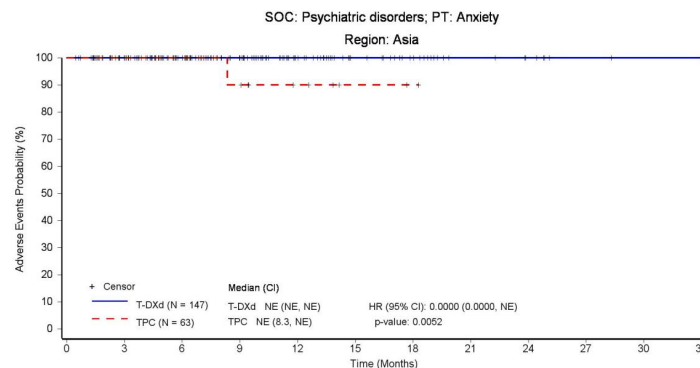
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:32; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PAT\_4\_SAS.rf

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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 147)	147	132	100	75	43	26	18	9	6	2	1	0
TPC (N = 63)	63	40	20	9	5	2	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

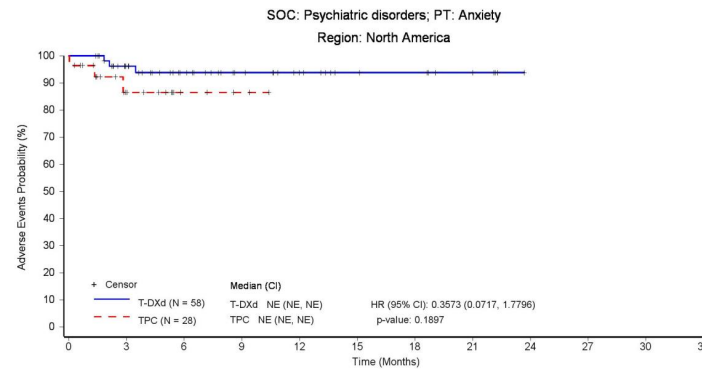
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 58)	58	43	31	22	15	9	8	4	0	0	0	0
TPC (N = 28)	28	13	4	2	0	0	0	0	0	0	0	0

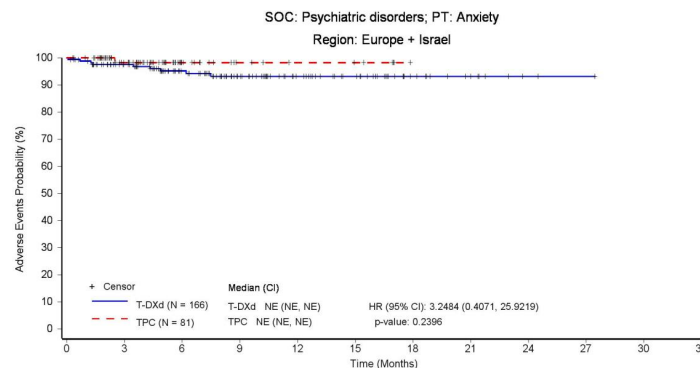
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 166)	166	134	98	69	45	33	15	7	2	1	0	0
TPC (N = 81)	81	51	19	9	6	5	0	0	0	0	0	0

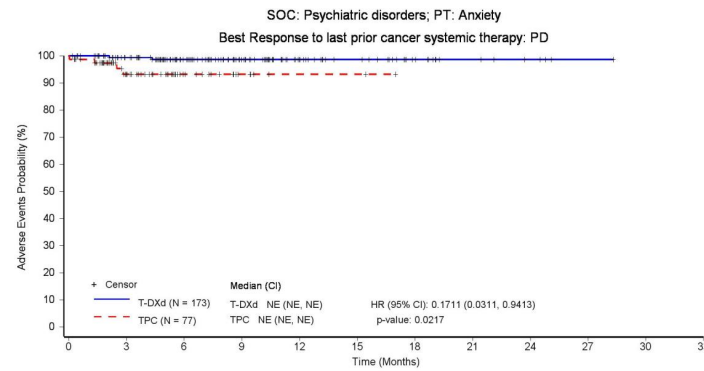
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

Time (Months)	T-DXd (N = 173)	TPC (N = 77)
0	173	77
3	143	42
6	101	17
9	70	6
12	39	2
15	27	2
18	15	0
21	7	0
24	4	0
27	1	0
30	0	0
33	0	0

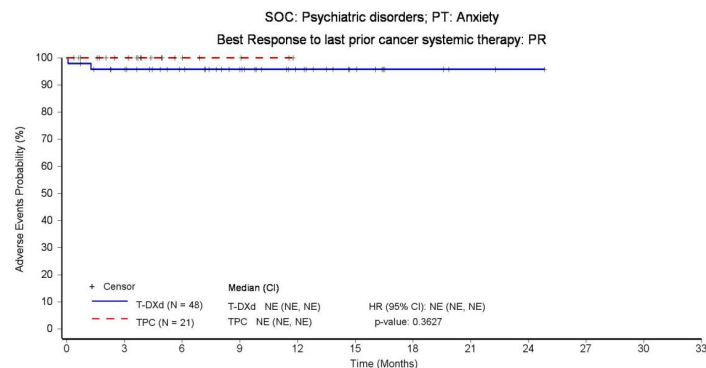
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

Time (Months)	T-DXd (N = 48)	TPC (N = 21)
0	48	21
3	42	14
6	34	5
9	26	3
12	16	0
15	9	0
18	4	0
21	2	0
24	1	0
27	0	0
30	0	0
33	0	0

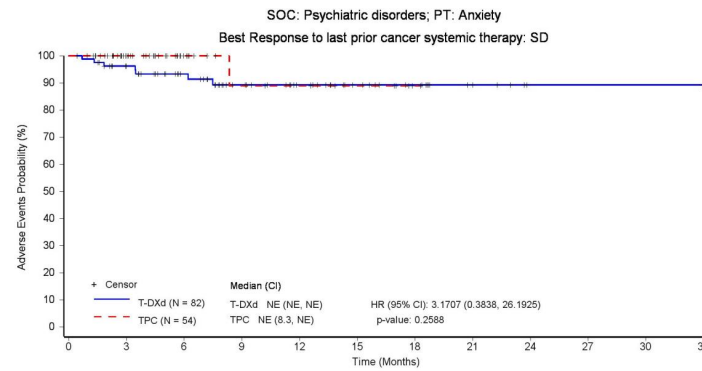
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 82)	82	65	49	35	26	17	12	5	1	1	1	0
TPC (N = 54)	54	35	16	8	7	5	1	0	0	0	0	0

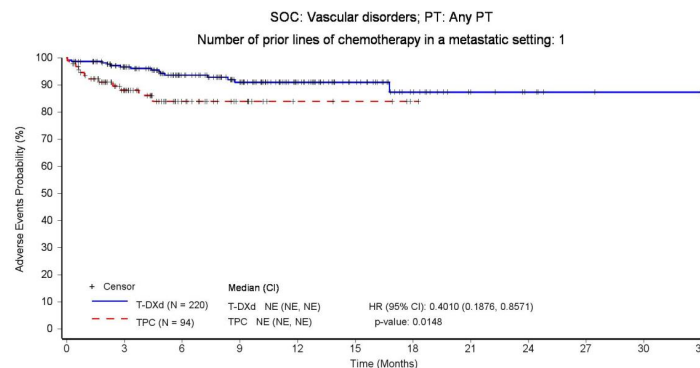
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 220)	220	179	130	97	60	37	18	8	5	2	1	0
TPC (N = 94)	94	54	24	12	5	4	1	0	0	0	0	0

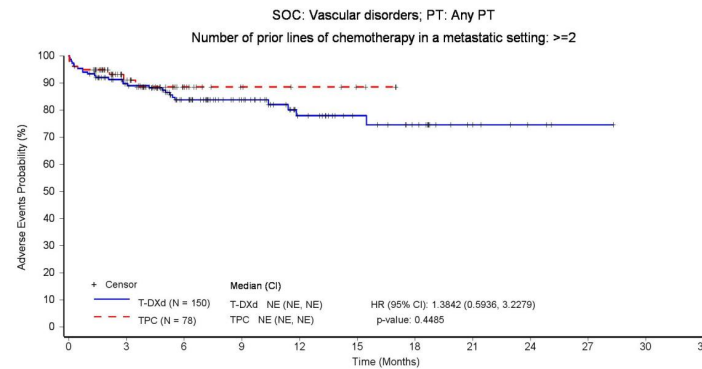
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 150)	150	118	84	58	35	23	16	6	3	1	0	0
TPC (N = 78)	78	42	16	7	5	3	0	0	0	0	0	0

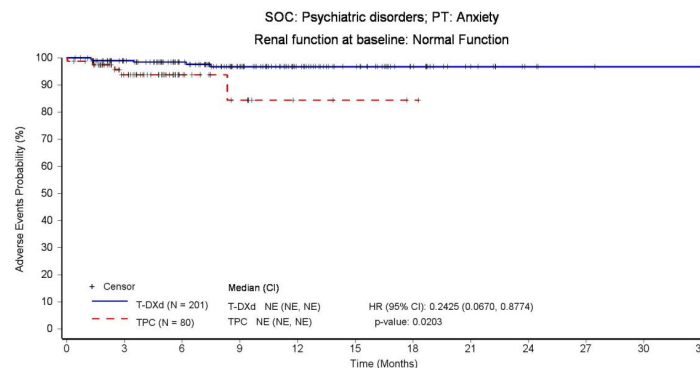
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 201)	201	171	126	91	56	39	22	10	4	2	1	0
TPC (N = 80)	80	46	17	8	3	2	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

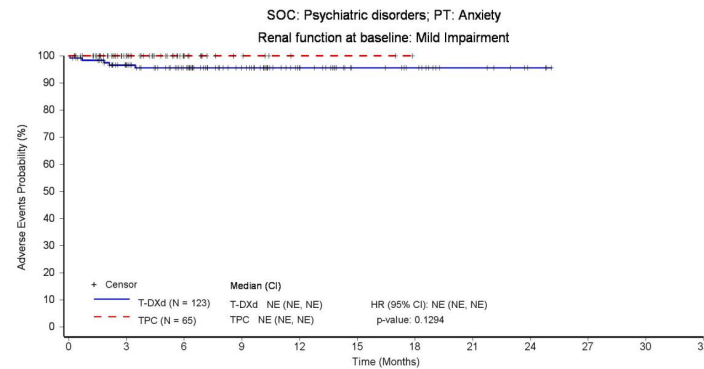
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 123)	123	99	76	54	33	19	15	8	3	0	0	0
TPC (N = 65)	65	38	15	6	2	2	0	0	0	0	0	0

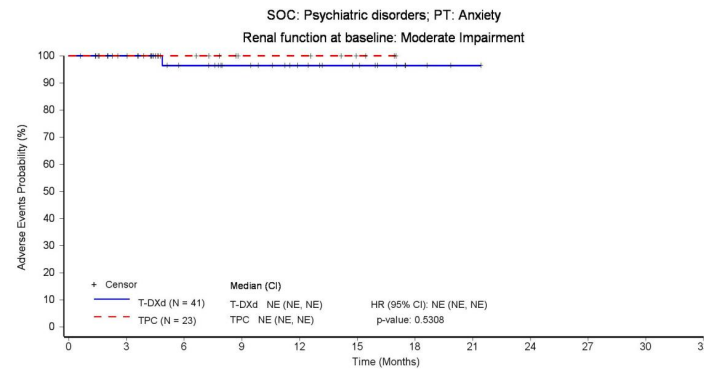
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 41)	41	35	25	19	13	9	3	1	0	0	0	0
TPC (N = 23)	23	18	11	6	6	3	0	0	0	0	0	0

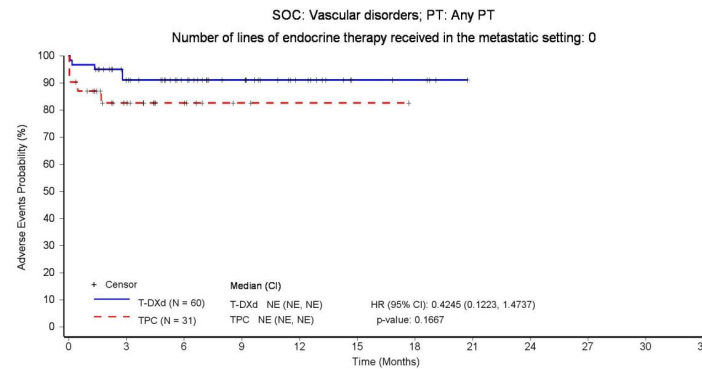
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 60)	60	46	32	23	13	5	4	0	0	0	0	0
TPC (N = 31)	31	14	7	2	1	1	0	0	0	0	0	0

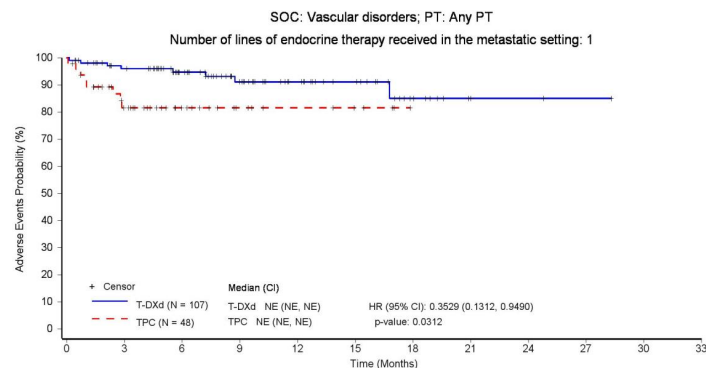
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 107)	107	89	66	45	30	21	9	2	2	1	0	0
TPC (N = 48)	48	30	16	9	6	4	0	0	0	0	0	0

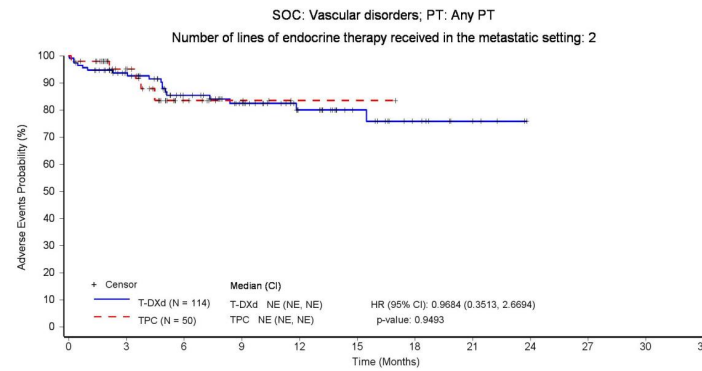
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 114)	114	87	64	48	31	19	10	4	0	0	0	0
TPC (N = 50)	50	29	9	4	1	1	0	0	0	0	0	0

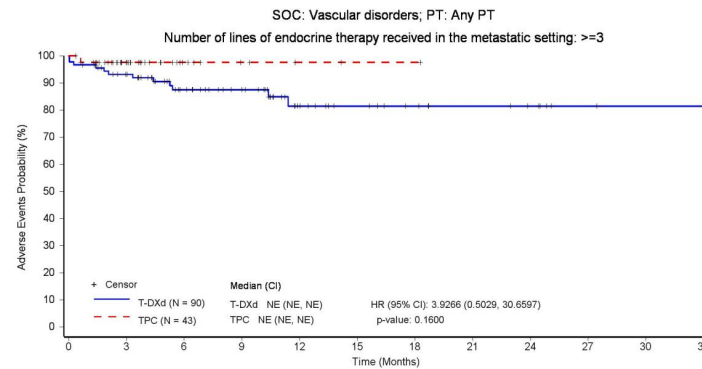
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:32; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PAT\_4\_SAS.rf

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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 90)	90	76	53	39	21	15	11	8	6	2	1	0
TPC (N = 43)	43	23	8	4	2	1	1	0	0	0	0	0

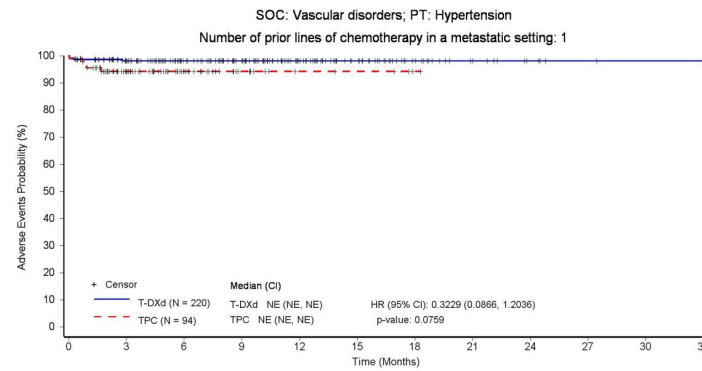
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 220)	220	182	136	106	67	43	21	10	5	2	1	0
TPC (N = 94)	94	58	27	12	5	4	1	0	0	0	0	0

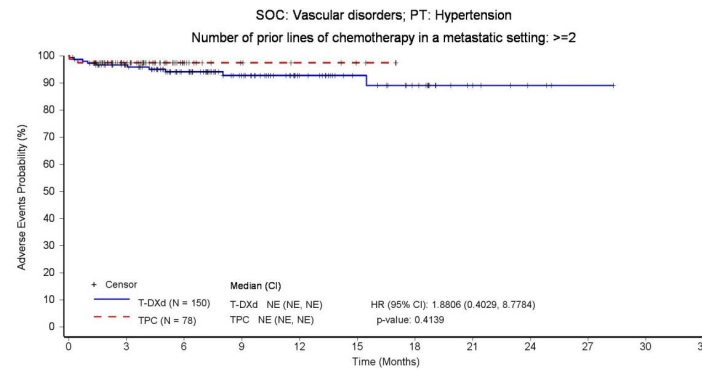
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:32; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PAT\_4\_SAS.rf

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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 150)	150	123	91	61	38	25	17	6	3	1	0	0
TPC (N = 78)	78	45	16	7	5	3	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

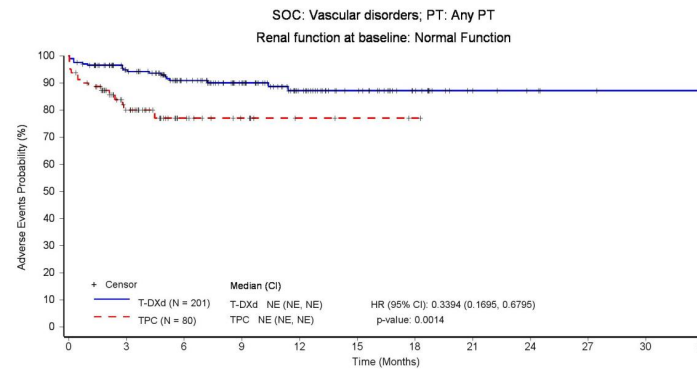
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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 201)	201	163	114	85	50	33	18	6	4	2	1	0
TPC (N = 80)	80	39	16	8	3	2	1	0	0	0	0	0

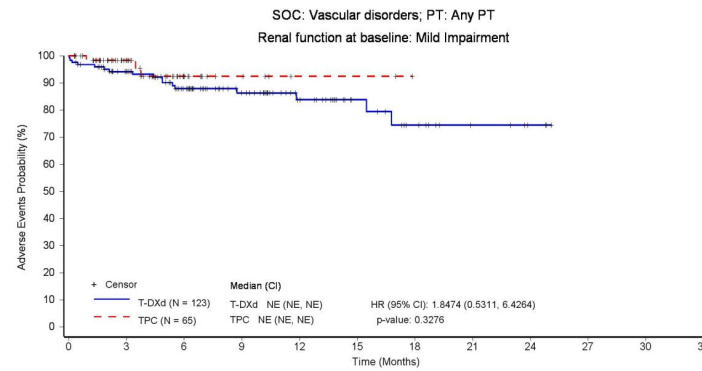
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 123)	123	100	75	52	33	19	12	6	3	0	0	0
TPC (N = 65)	65	38	14	6	2	2	0	0	0	0	0	0

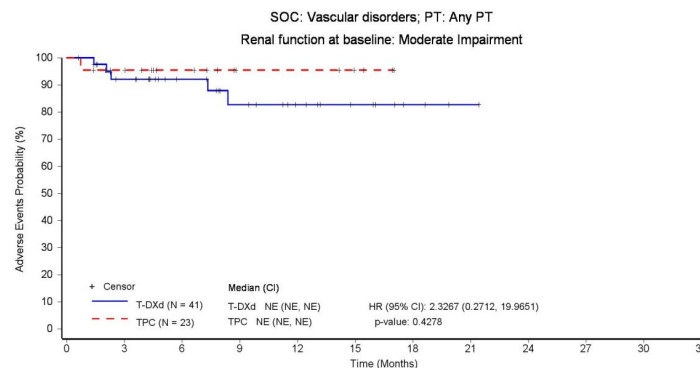
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 41)	41	32	23	16	11	7	3	1	0	0	0	0
TPC (N = 23)	23	17	10	5	5	3	0	0	0	0	0	0

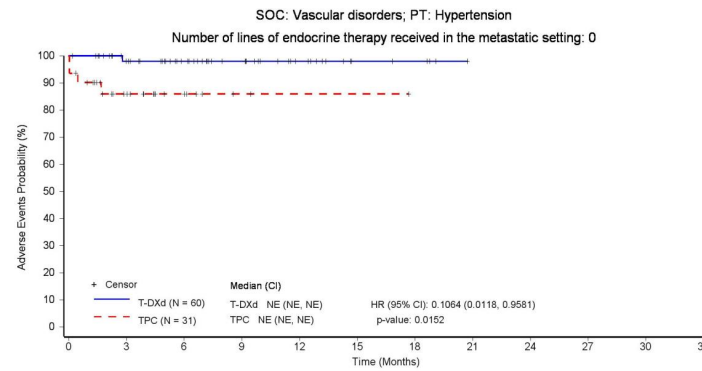
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 60)	60	48	33	23	13	5	4	0	0	0	0	0
TPC (N = 31)	31	15	7	2	1	1	0	0	0	0	0	0

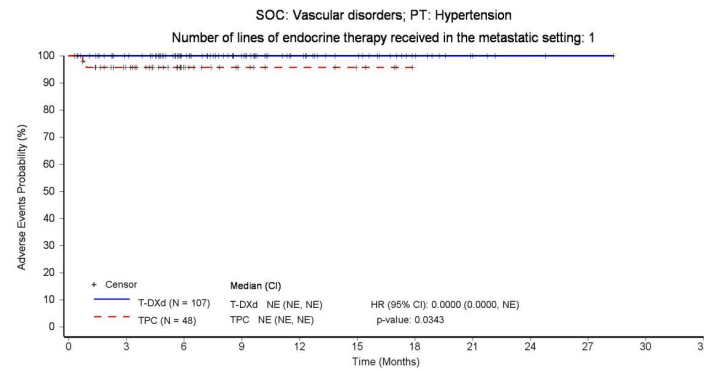
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 107)	107	91	67	47	31	22	11	4	2	1	0	0
TPC (N = 48)	48	35	17	9	6	4	0	0	0	0	0	0

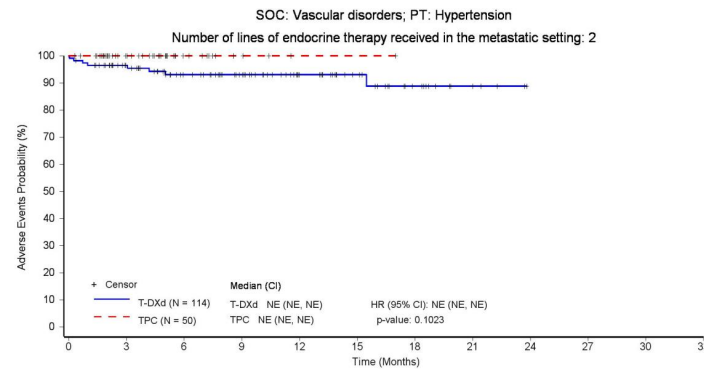
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 114)	114	89	70	56	37	24	12	4	0	0	0	0
TPC (N = 50)	50	30	11	4	1	1	0	0	0	0	0	0

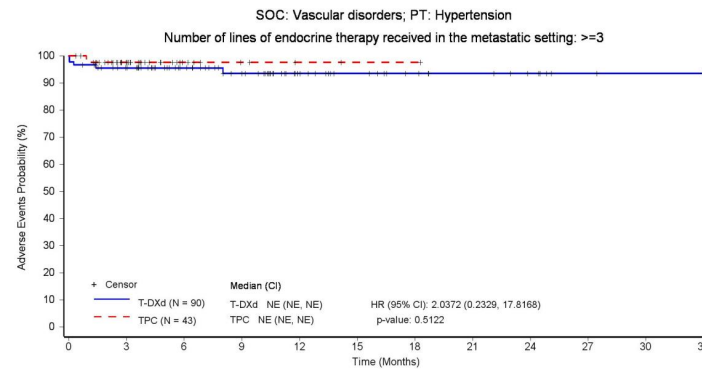
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 90)	90	78	58	42	25	18	12	9	6	2	1	0
TPC (N = 43)	43	23	8	4	2	1	1	0	0	0	0	0

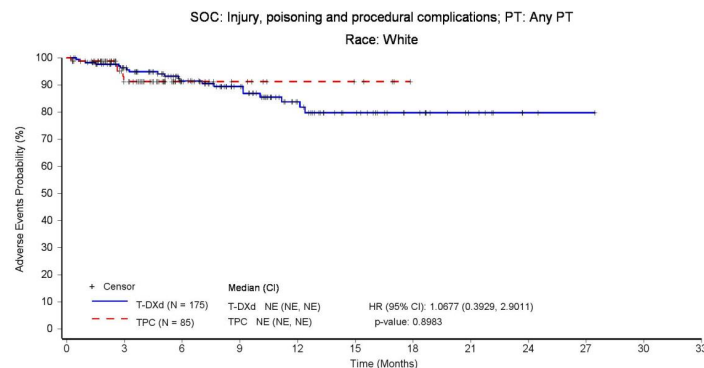
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 175)	175	137	99	73	42	28	16	8	2	1	0	0
TPC (N = 85)	85	46	18	9	5	4	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

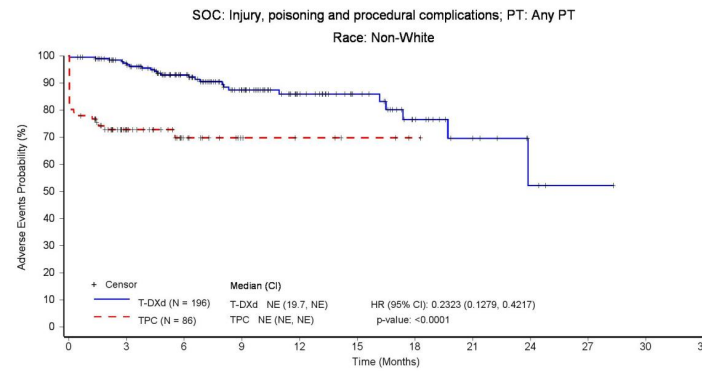
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 196)	196	167	119	80	47	33	18	8	3	1	0	0
TPC (N = 86)	86	39	16	7	5	3	1	0	0	0	0	0

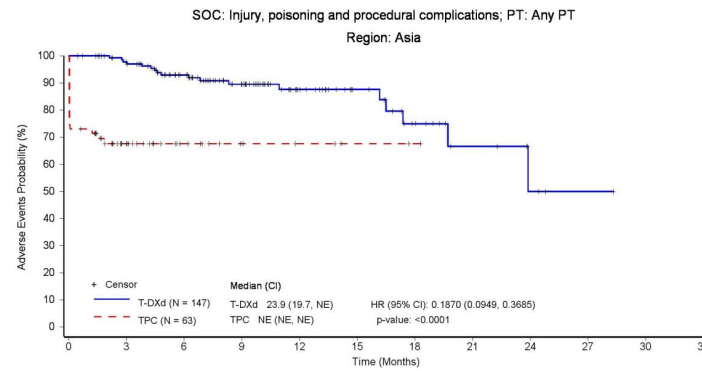
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 147)	147	129	93	66	37	24	14	7	3	1	0	0
TPC (N = 63)	63	25	12	6	4	2	1	0	0	0	0	0

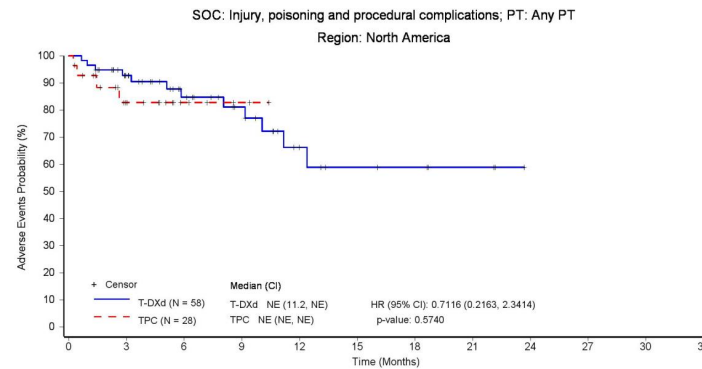
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 58)	58	42	28	20	9	6	5	3	0	0	0	0
TPC (N = 28)	28	13	5	2	0	0	0	0	0	0	0	0

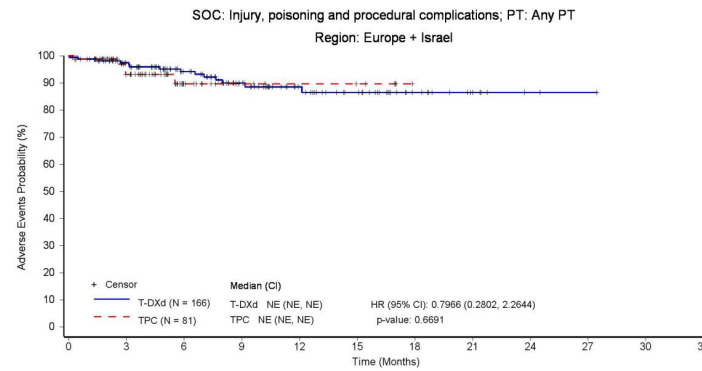
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 166)	166	133	97	67	43	31	15	6	2	1	0	0
TPC (N = 81)	81	48	17	8	6	5	0	0	0	0	0	0

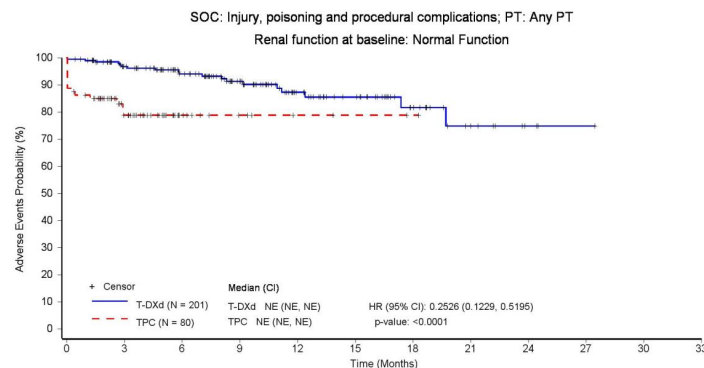
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 201)	201	167	121	87	51	37	19	8	3	1	0	0
TPC (N = 80)	80	36	12	6	3	2	1	0	0	0	0	0

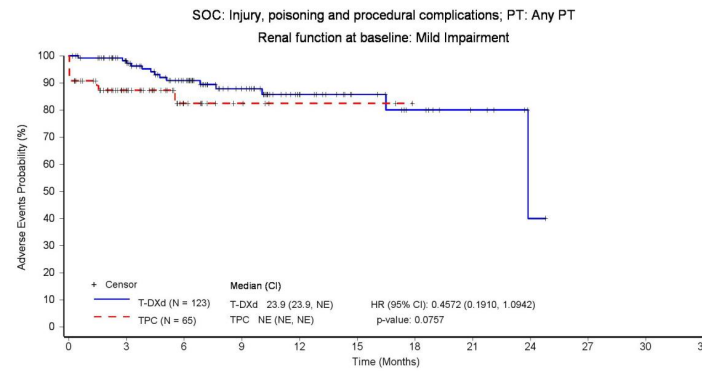
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:32; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PAT\_4\_SAS.rf

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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 123)	123	101	73	49	27	17	11	6	1	0	0	0
TPC (N = 65)	65	34	12	5	2	2	0	0	0	0	0	0

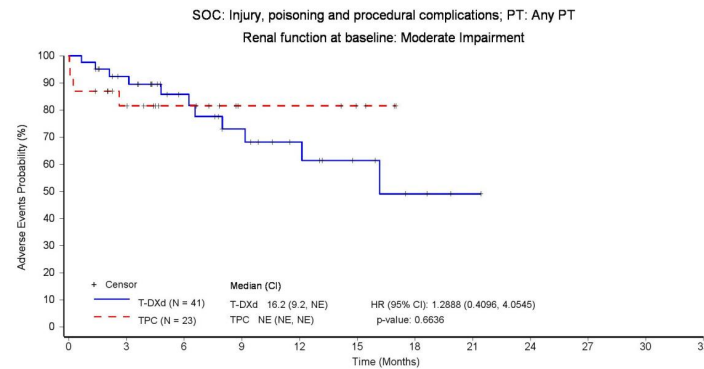
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 41)	41	32	21	15	10	6	3	1	0	0	0	0
TPC (N = 23)	23	15	10	5	5	3	0	0	0	0	0	0

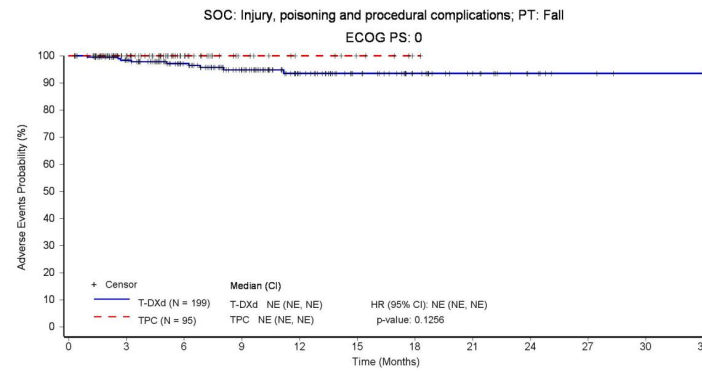
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:32; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PAT\_4\_SAS.rf

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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 199)	199	176	135	102	62	42	26	15	7	3	1	0
TPC (N = 95)	95	58	29	13	8	5	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

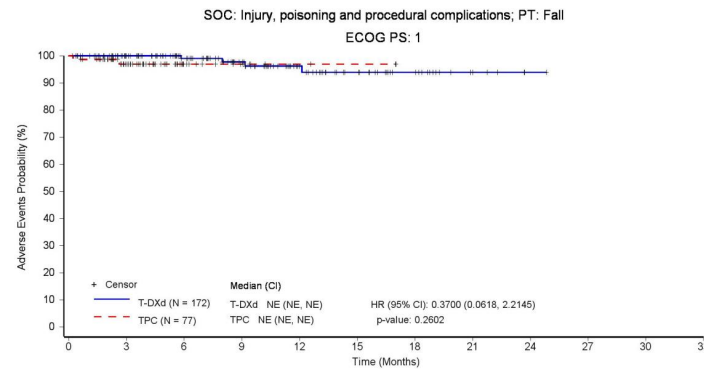
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 Run date: 21OCT2022 – 17:32; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PAT\_4\_SAS.rf



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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

T-DXd (N = 172)	172	136	98	67	41	27	16	5	1	0	0	0
TPC (N = 77)	77	48	15	7	3	2	0	0	0	0	0	0

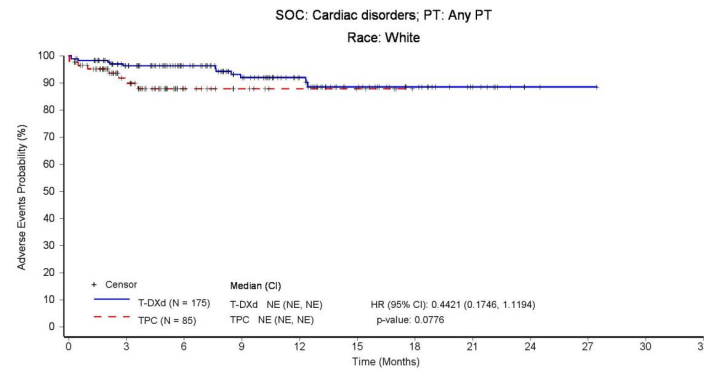
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 175)	175	139	106	78	54	34	20	10	2	1	0	0
TPC (N = 85)	85	49	17	9	5	4	0	0	0	0	0	0

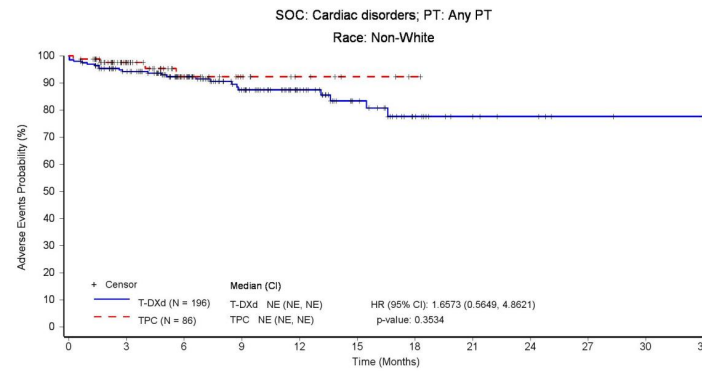
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 196)	196	164	120	82	52	32	16	7	5	2	1	0
TPC (N = 86)	86	54	23	11	6	3	1	0	0	0	0	0

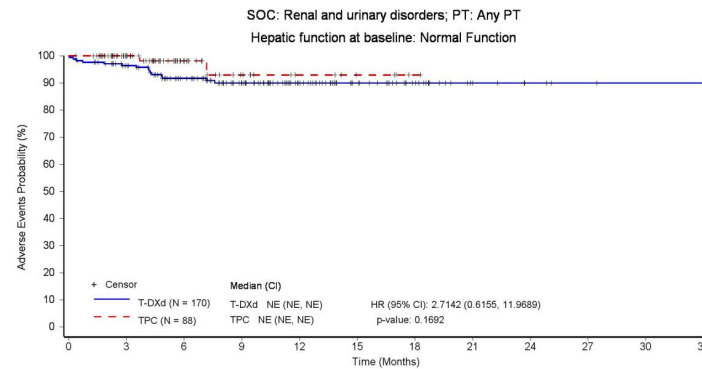
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 170)	170	150	118	90	55	34	20	7	4	2	1	0
TPC (N = 88)	88	61	27	13	7	4	1	0	0	0	0	0

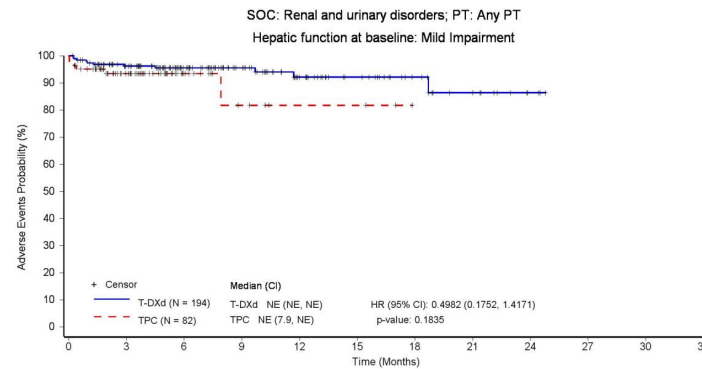
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 194)	194	151	105	71	44	30	19	10	3	0	0	0
TPC (N = 82)	82	46	16	6	3	3	0	0	0	0	0	0

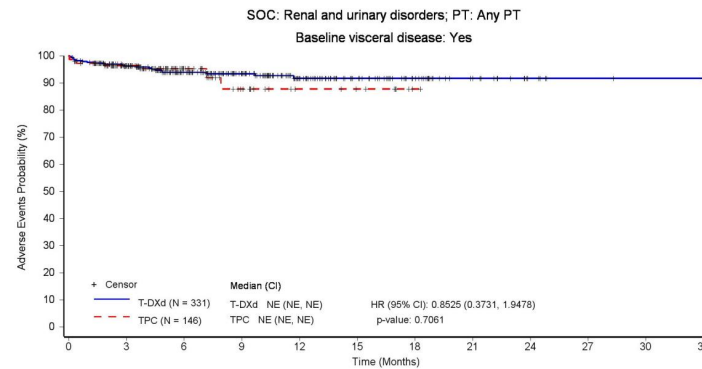
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 331)	331	269	198	144	89	57	34	16	6	2	1	0
TPC (N = 146)	146	93	38	18	9	7	1	0	0	0	0	0

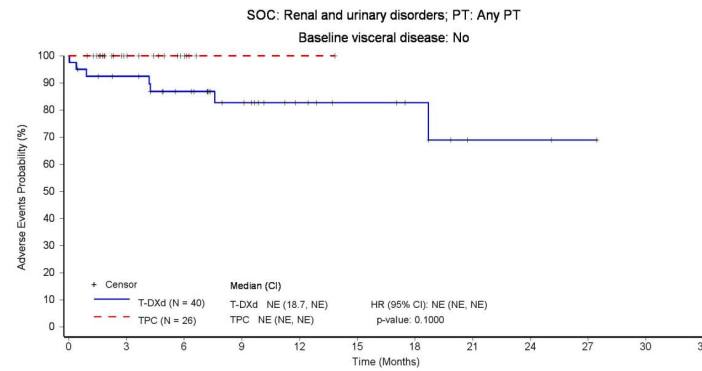
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 40)	40	34	27	19	11	8	6	2	2	1	0	0
TPC (N = 26)	26	14	5	1	1	0	0	0	0	0	0	0

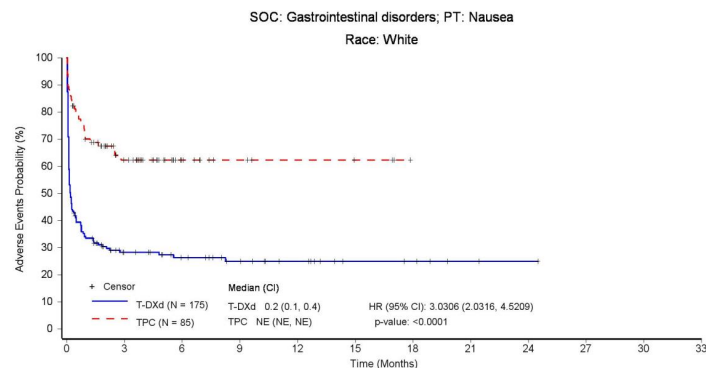
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:32; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PAT\_4\_SAS.rf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 175)	175	34	25	17	12	6	5	2	1	0	0	0
TPC (N = 85)	85	34	12	6	4	3	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

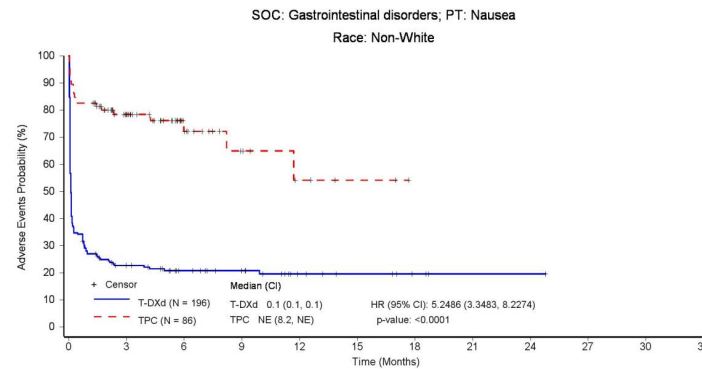
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 196)	196	39	27	20	10	7	3	1	1	0	0	0
TPC (N = 86)	86	45	18	8	4	2	0	0	0	0	0	0

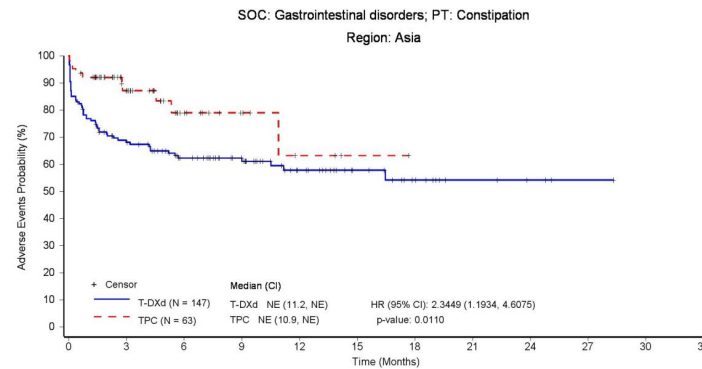
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:32; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PAT\_4\_SAS.rf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 147)	147	89	64	50	29	18	11	5	3	1	0	0
TPC (N = 63)	63	34	14	7	3	1	0	0	0	0	0	0

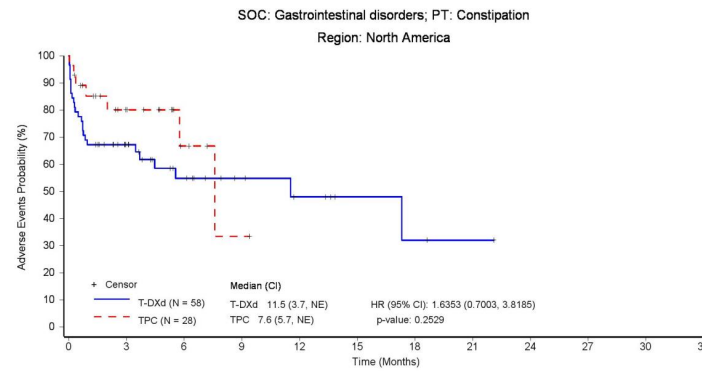
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 58)	58	27	15	9	6	3	2	1	0	0	0	0
TPC (N = 28)	28	13	4	1	0	0	0	0	0	0	0	0

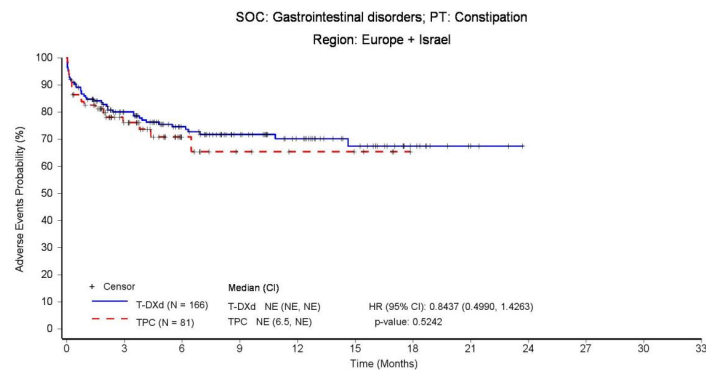
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 166)	166	109	80	57	39	25	12	3	0	0	0	0
TPC (N = 81)	81	38	13	7	5	4	0	0	0	0	0	0

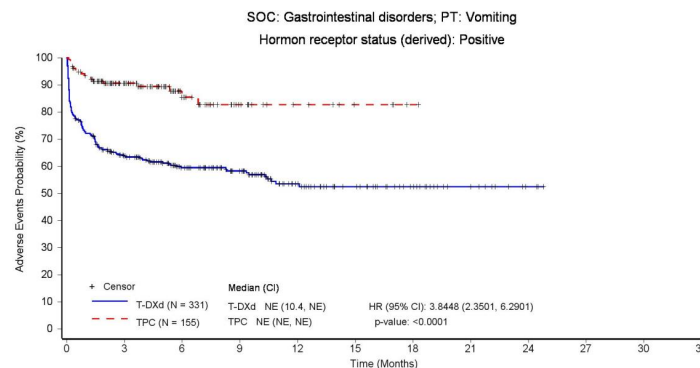
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 331)	331	183	131	92	51	35	22	10	3	0	0	0
TPC (N = 155)	155	90	36	16	8	4	1	0	0	0	0	0

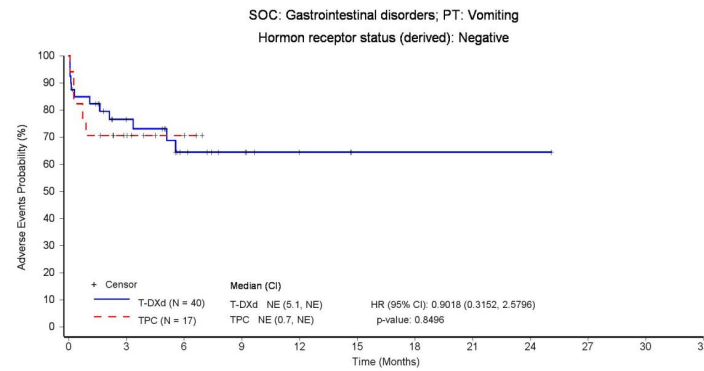
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 40)	40	22	11	7	3	1	1	1	1	0	0	0
TPC (N = 17)	17	7	3	0	0	0	0	0	0	0	0	0

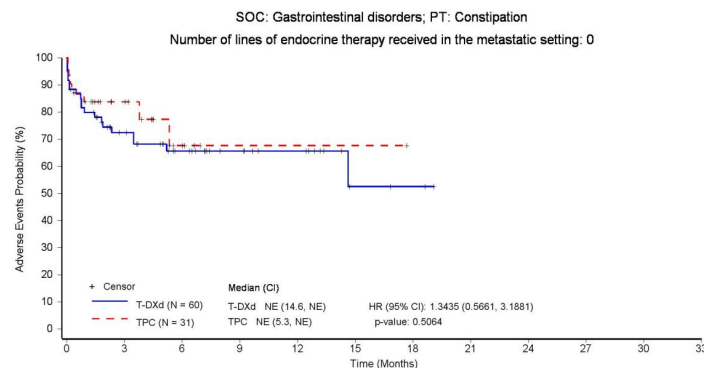
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:32; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PAT\_4\_SAS.rf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 60)	60	35	23	15	11	3	2	0	0	0	0	0
TPC (N = 31)	31	15	5	1	1	1	0	0	0	0	0	0

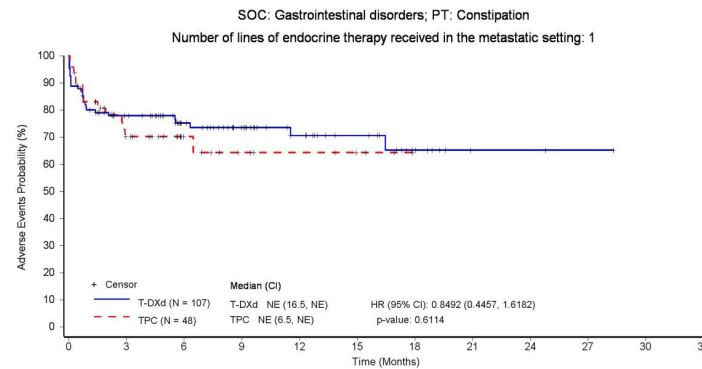
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 107)	107	69	48	35	23	16	8	2	2	1	0	0
TPC (N = 48)	48	25	12	7	5	3	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

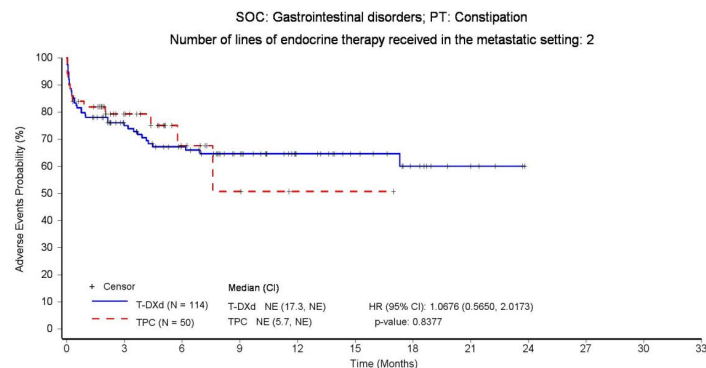
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 114)	114	69	54	40	25	17	10	4	0	0	0	0
TPC (N = 50)	50	23	8	3	1	1	0	0	0	0	0	0

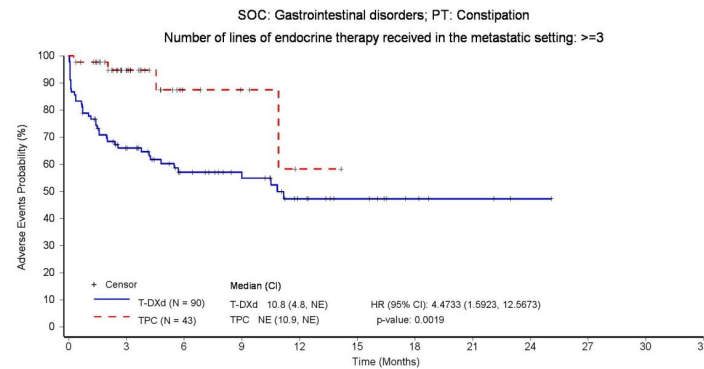
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 90)	90	52	34	26	15	10	5	3	1	0	0	0
TPC (N = 43)	43	22	6	4	1	0	0	0	0	0	0	0

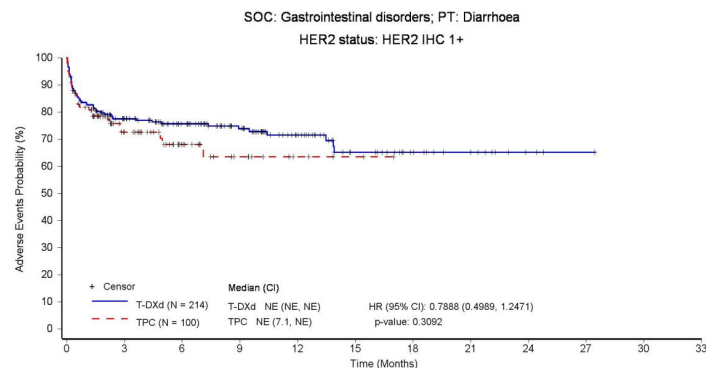
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 214)	214	137	104	76	46	26	16	9	3	1	0	0
TPC (N = 100)	100	43	21	10	4	2	0	0	0	0	0	0

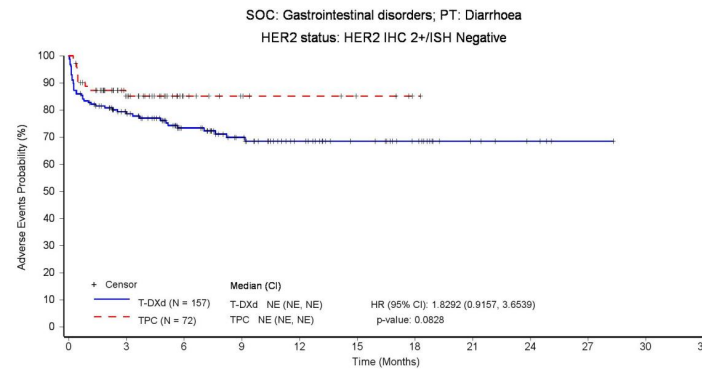
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 157)	157	103	71	52	33	23	16	7	4	1	0	0
TPC (N = 72)	72	39	13	8	6	4	1	0	0	0	0	0

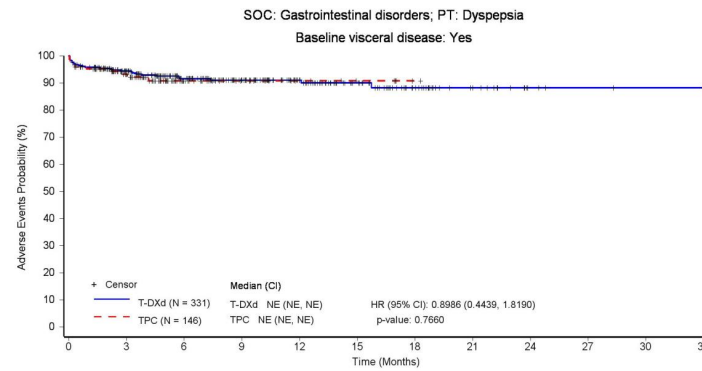
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 331)	331	261	187	134	89	57	31	14	4	2	1	0
TPC (N = 146)	146	86	32	15	8	5	1	0	0	0	0	0

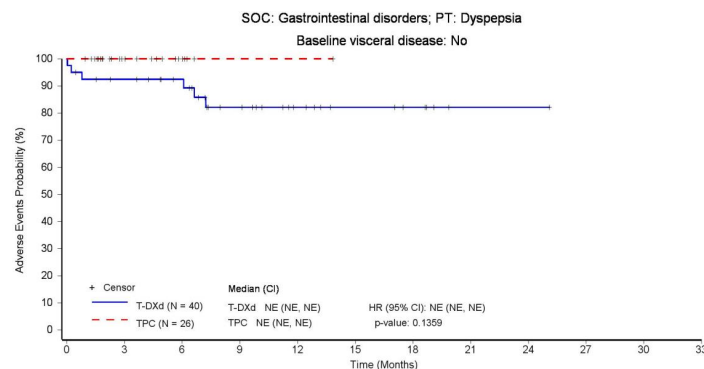
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 40)	40	34	29	19	11	7	5	1	1	0	0	0
TPC (N = 26)	26	14	5	1	1	0	0	0	0	0	0	0

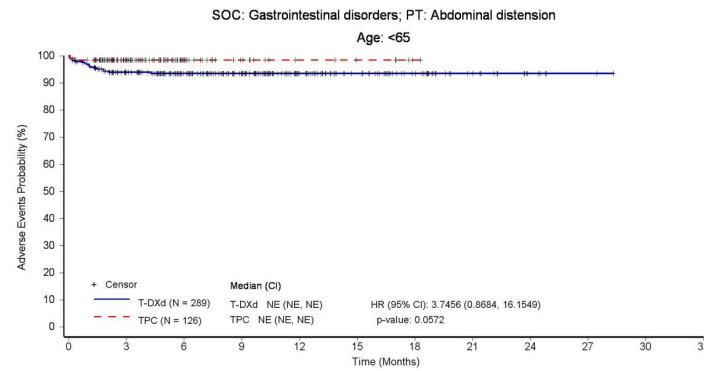
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 289)	289	233	176	131	79	54	34	15	6	2	0	0
TPC (N = 126)	126	71	29	14	7	5	1	0	0	0	0	0

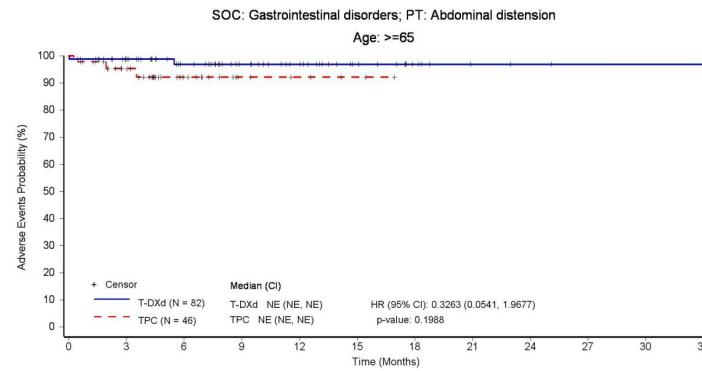
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 82)	82	64	47	33	25	15	7	3	2	1	1	0
TPC (N = 46)	46	33	15	6	4	2	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

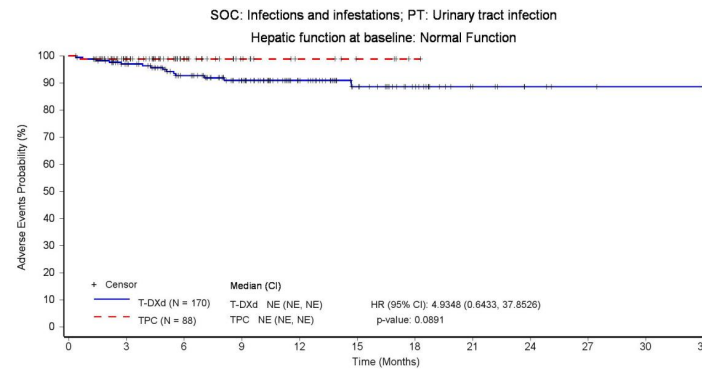
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 170)	170	151	119	92	58	36	20	8	4	2	1	0
TPC (N = 88)	88	61	28	13	7	4	1	0	0	0	0	0

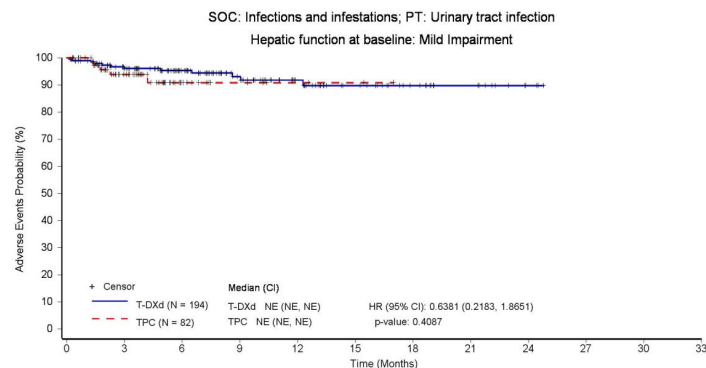
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 194)	194	150	107	70	46	29	19	11	3	0	0	0
TPC (N = 82)	82	44	14	6	3	2	0	0	0	0	0	0

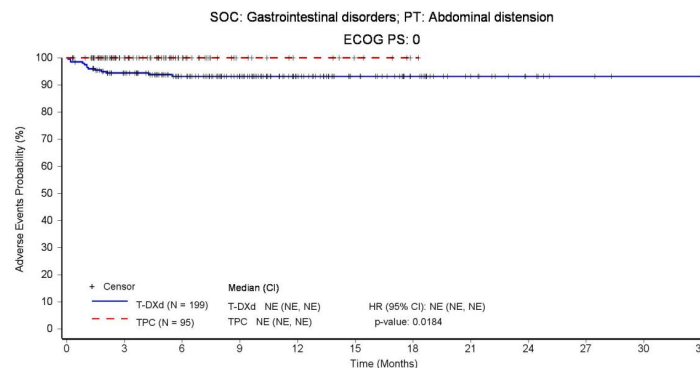
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 199)	199	168	130	100	64	44	27	14	7	3	1	0
TPC (N = 95)	95	58	29	13	8	5	1	0	0	0	0	0

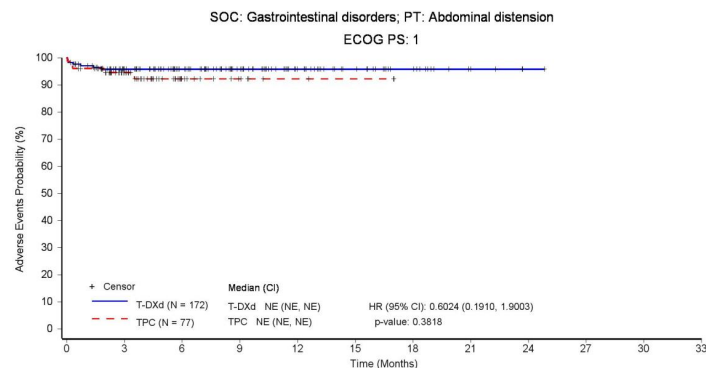
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 172)	172	129	93	64	40	25	14	4	1	0	0	0
TPC (N = 77)	77	46	15	7	3	2	0	0	0	0	0	0

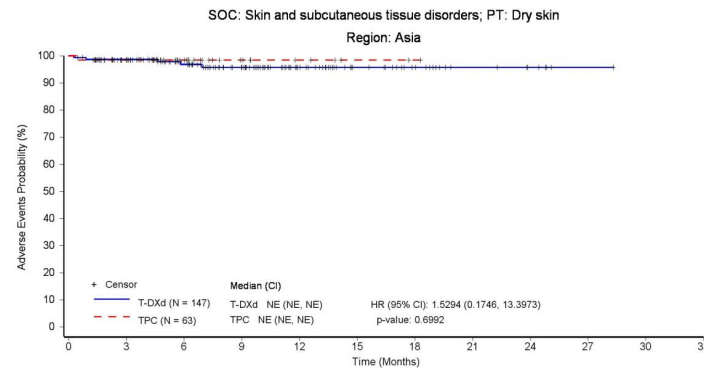
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 147)	147	130	97	72	41	24	16	8	5	1	0	0
TPC (N = 63)	63	40	20	9	5	2	1	0	0	0	0	0

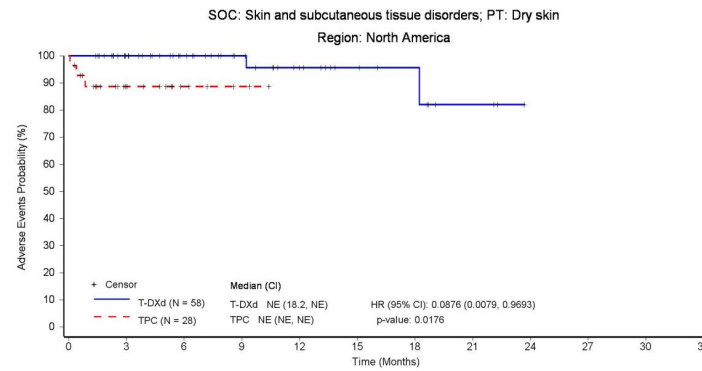
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 58)	58	45	34	25	16	10	7	3	0	0	0	0
TPC (N = 28)	28	12	5	2	0	0	0	0	0	0	0	0

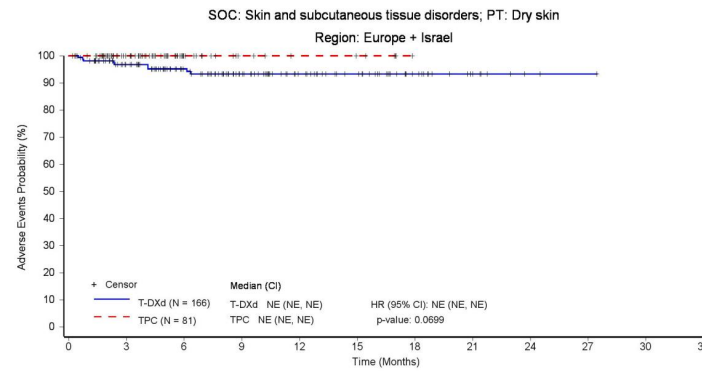
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 166)	166	132	100	71	48	36	18	7	2	1	0	0
TPC (N = 81)	81	52	19	9	6	5	0	0	0	0	0	0

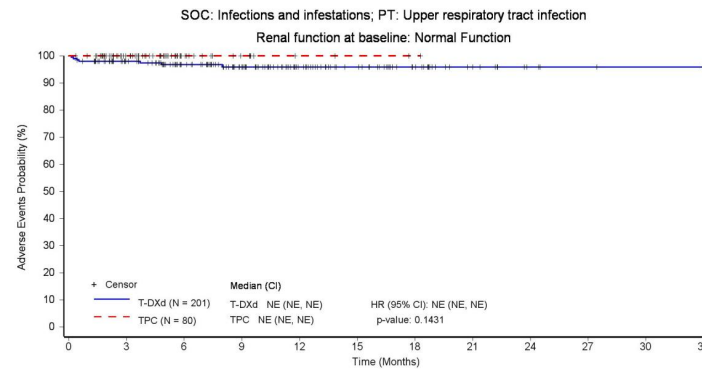
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 201)	201	169	125	93	57	40	24	10	4	2	1	0
TPC (N = 80)	80	49	18	8	3	2	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

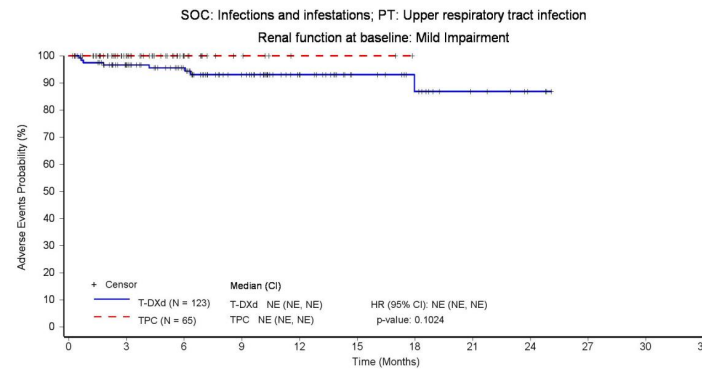
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 123)	123	99	78	55	35	21	14	7	3	0	0	0
TPC (N = 65)	65	38	15	6	2	2	0	0	0	0	0	0

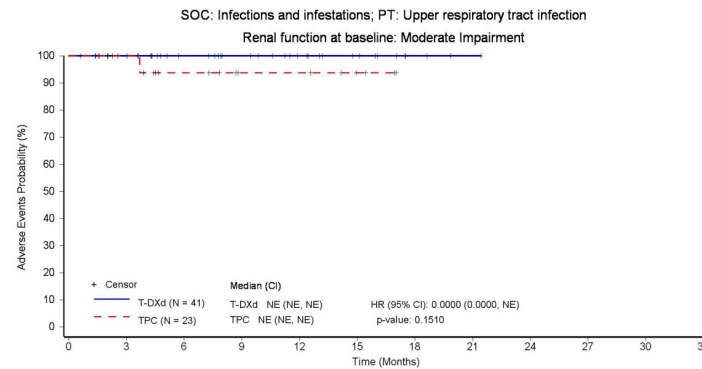
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 41)	41	35	26	20	14	9	3	1	0	0	0	0
TPC (N = 23)	23	18	10	6	6	3	0	0	0	0	0	0

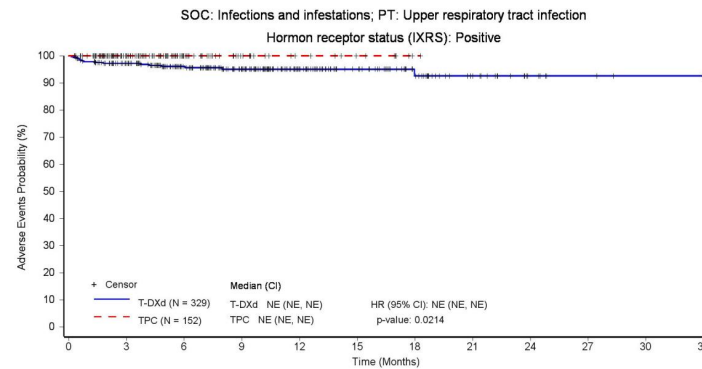
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 329)	329	276	212	157	99	66	38	18	7	3	1	0
TPC (N = 152)	152	96	41	20	11	7	1	0	0	0	0	0

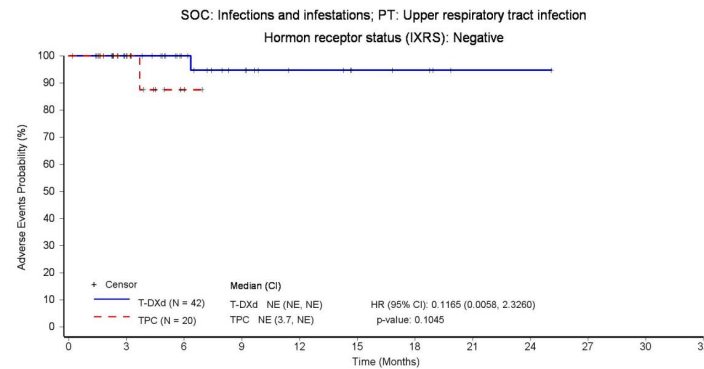
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 42)	42	31	20	13	8	5	4	1	1	0	0	0
TPC (N = 20)	20	12	2	0	0	0	0	0	0	0	0	0

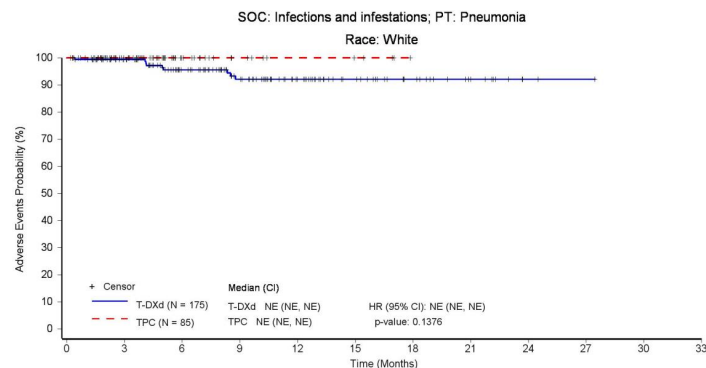
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 175)	175	142	107	77	50	32	18	9	2	1	0	0
TPC (N = 85)	85	50	19	9	5	4	0	0	0	0	0	0

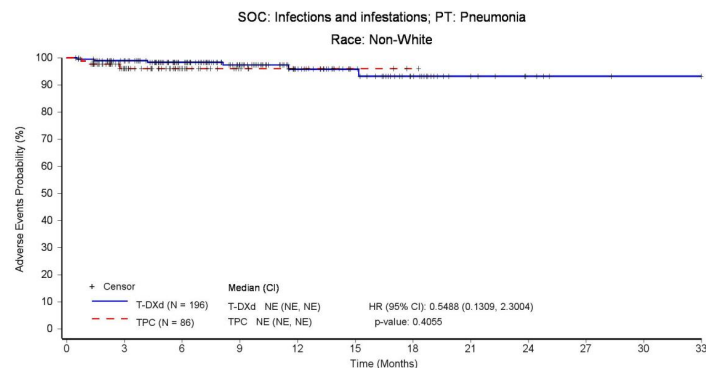
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 196)	196	171	128	91	55	38	22	9	5	2	1	0
TPC (N = 86)	86	54	25	11	6	3	1	0	0	0	0	0

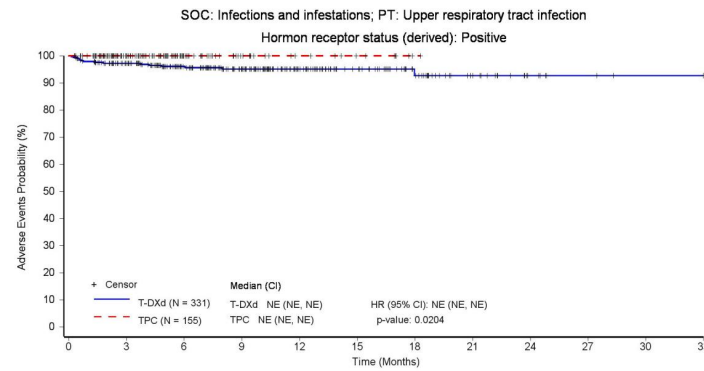
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 331)	331	277	212	158	100	67	39	18	7	3	1	0
TPC (N = 155)	155	98	41	20	11	7	1	0	0	0	0	0

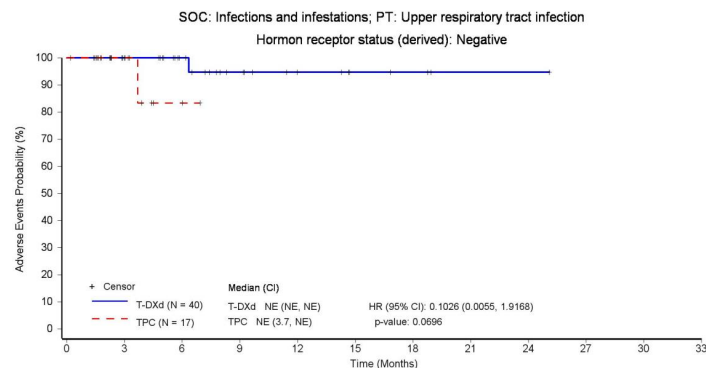
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 40)	40	30	20	12	7	4	3	1	1	0	0	0
TPC (N = 17)	17	9	2	0	0	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

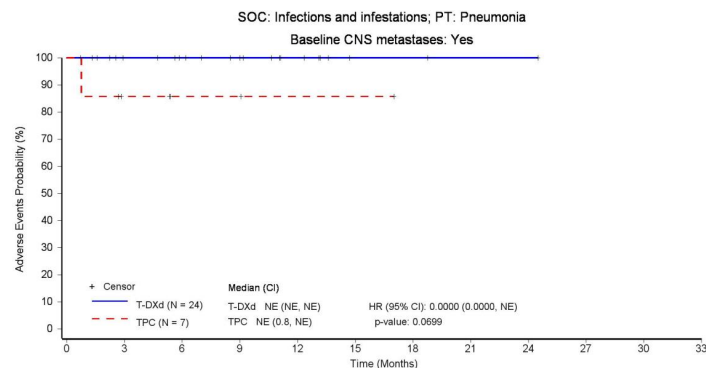
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 24)	24	18	15	12	7	2	2	1	1	0	0	0
TPC (N = 7)	7	4	2	2	1	1	0	0	0	0	0	0

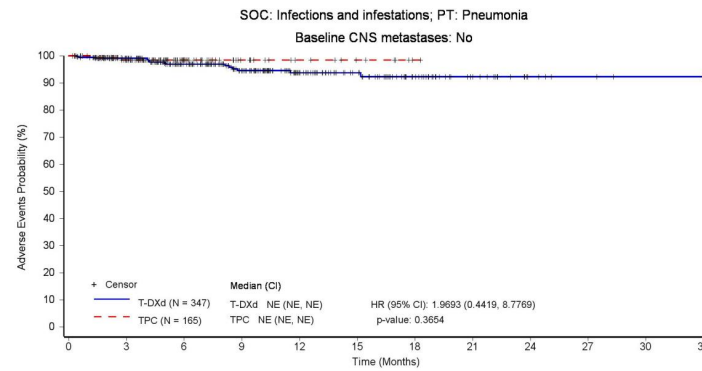
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

Time (Months)	T-DXd (N = 347)	TPC (N = 165)
0	347	165
3	295	101
6	220	42
9	156	18
12	98	10
15	68	6
18	38	1
21	17	0
24	6	0
27	3	0
30	1	0
33	0	0

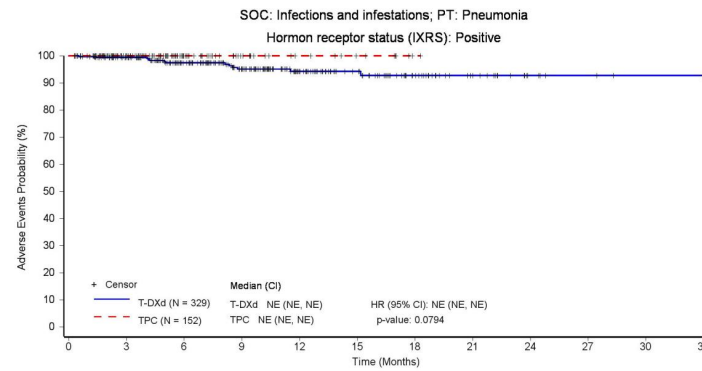
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

Time (Months)	T-DXd (N = 329)	TPC (N = 152)
0	329	152
3	282	96
6	215	41
9	155	20
12	97	11
15	65	7
18	36	1
21	17	0
24	6	0
27	3	0
30	1	0
33	0	0

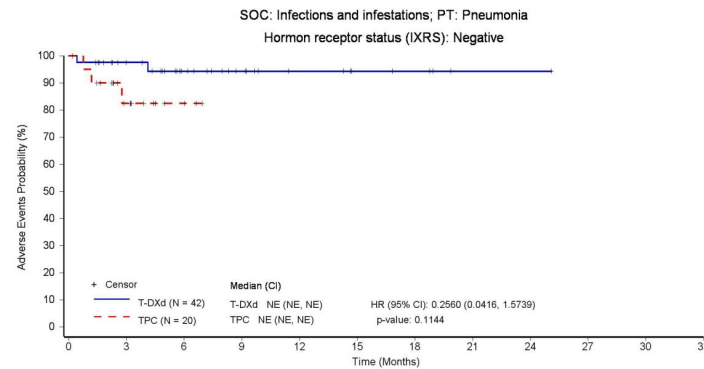
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Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 42)	42	31	20	13	8	5	4	1	1	0	0	0
TPC (N = 20)	20	10	3	0	0	0	0	0	0	0	0	0

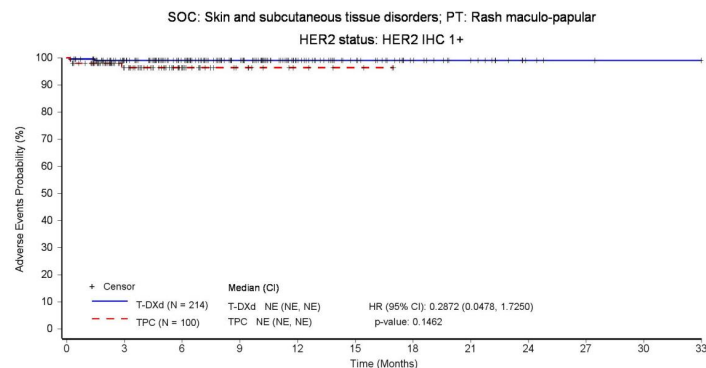
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 214)	214	176	137	100	61	39	23	13	4	2	1	0
TPC (N = 100)	100	58	26	11	5	3	0	0	0	0	0	0

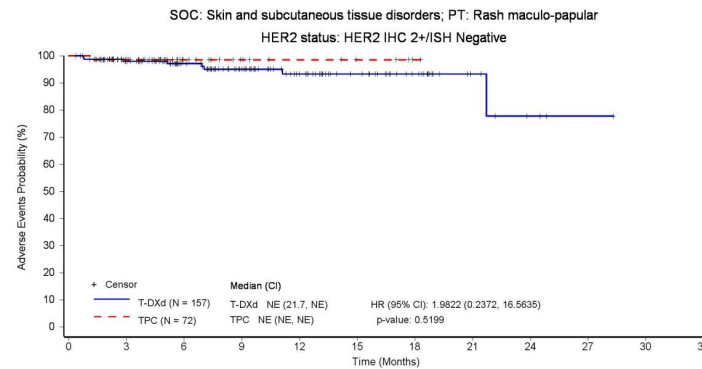
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

Time (Months)	T-DXd (N = 157)	TPC (N = 72)
0	157	72
3	133	46
6	97	17
9	71	9
12	46	6
15	31	4
18	19	1
21	7	0
24	3	0
27	1	0
30	0	0
33	0	0

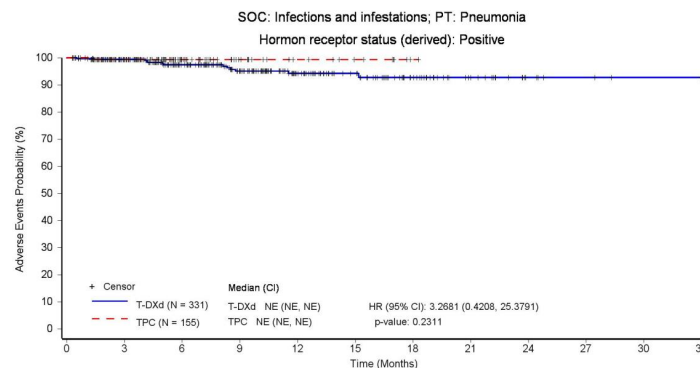
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 331)	331	283	215	156	98	66	37	17	6	3	1	0
TPC (N = 155)	155	97	41	20	11	7	1	0	0	0	0	0

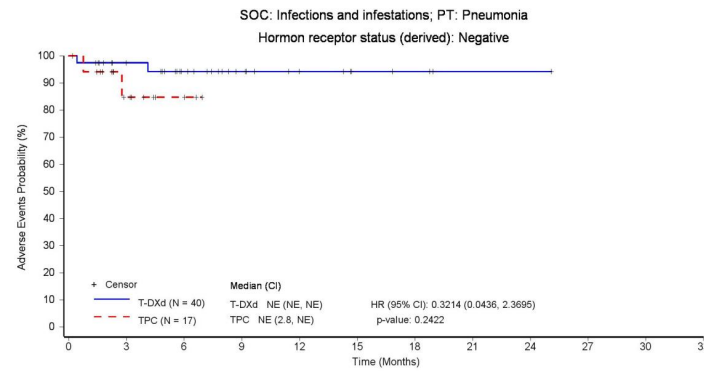
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:32; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PAT\_4\_SAS.rf

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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 40)	40	30	20	12	7	4	3	1	1	0	0	0
TPC (N = 17)	17	8	3	0	0	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

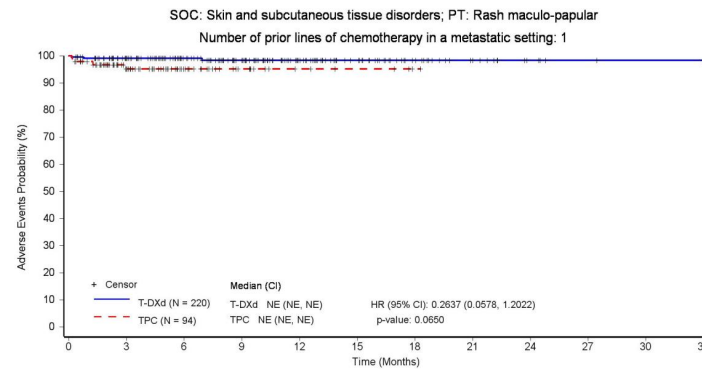
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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 220)	220	184	137	105	67	44	23	12	5	2	1	0
TPC (N = 94)	94	58	27	13	6	4	1	0	0	0	0	0

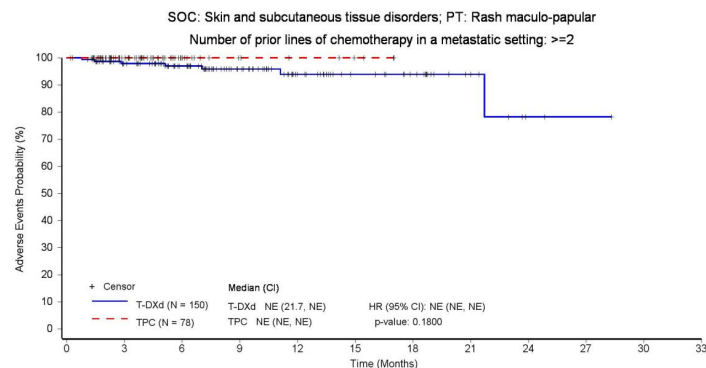
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 150)	150	124	96	65	39	25	18	7	2	1	0	0
TPC (N = 78)	78	46	16	7	5	3	0	0	0	0	0	0

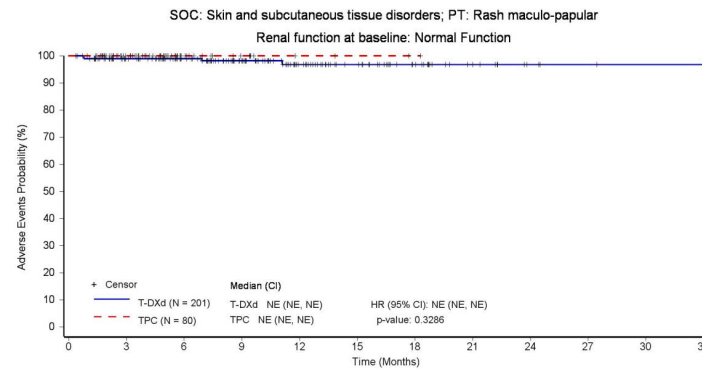
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:32; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PAT\_4\_SAS.rf

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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 201)	201	170	127	93	57	39	23	10	4	2	1	0
TPC (N = 80)	80	49	18	8	3	2	1	0	0	0	0	0

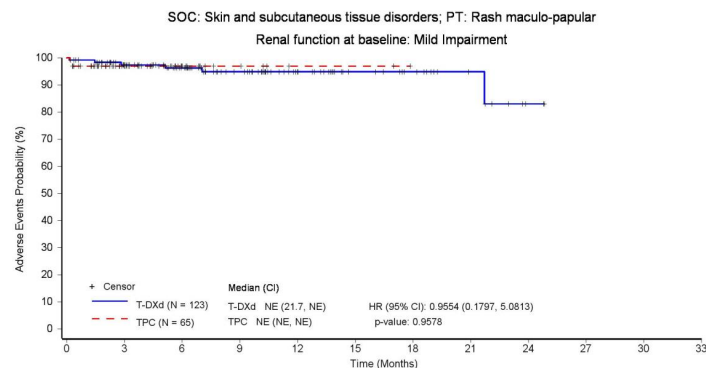
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:32; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PAT\_4\_SAS.rf

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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 123)	123	100	78	56	35	21	15	8	2	0	0	0
TPC (N = 65)	65	37	14	6	2	2	0	0	0	0	0	0

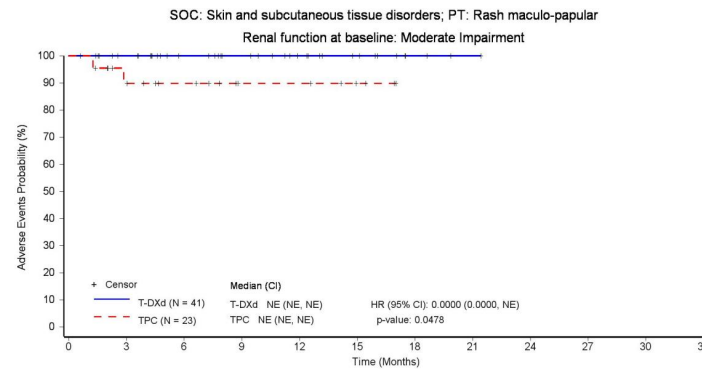
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:32; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PAT\_4\_SAS.rf

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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 41)	41	35	26	20	14	9	3	1	0	0	0	0
TPC (N = 23)	23	16	11	6	6	3	0	0	0	0	0	0

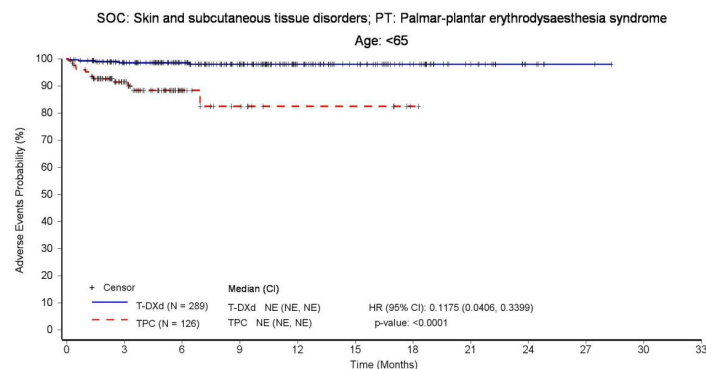
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:32; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PAT\_4\_SAS.rf

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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 289)	289	245	186	137	83	57	36	17	6	2	0	0
TPC (N = 126)	126	66	22	10	5	5	1	0	0	0	0	0

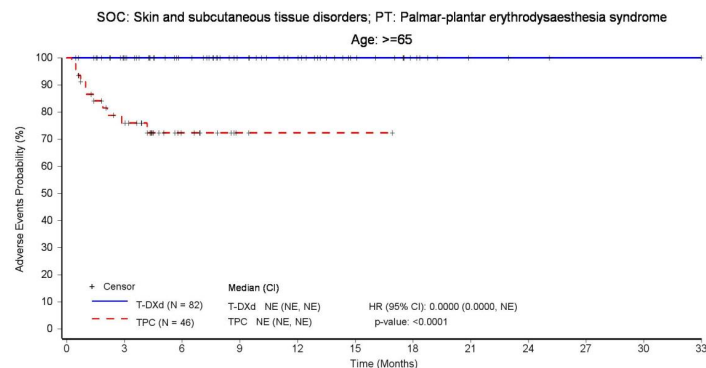
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 82)	82	65	49	35	27	16	8	3	2	1	1	0
TPC (N = 46)	46	27	9	2	1	1	0	0	0	0	0	0

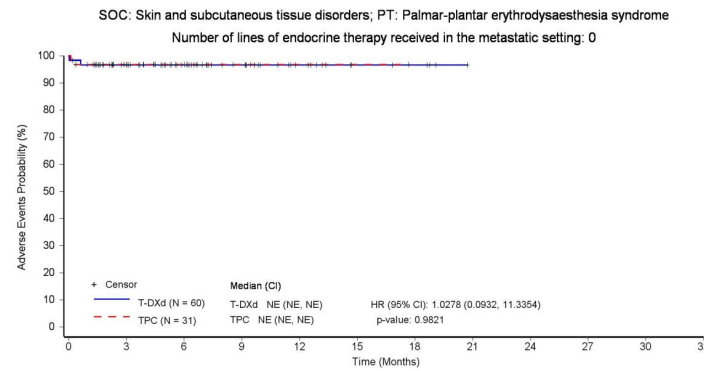
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 60)	60	47	33	22	12	5	4	0	0	0	0	0
TPC (N = 31)	31	17	7	2	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

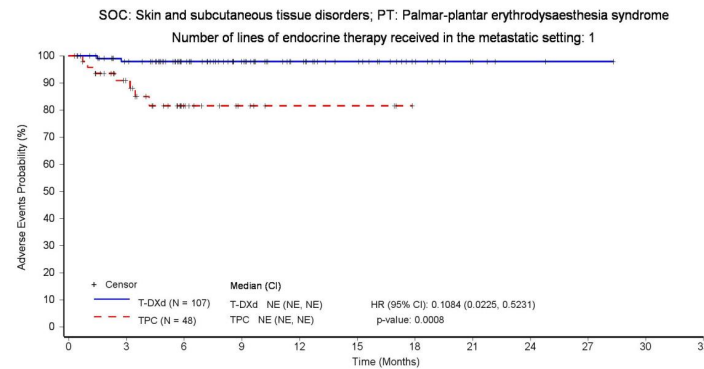
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 Run date: 21OCT2022 – 17:32; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PAT\_4\_SAS.rf



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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 107)	107	89	65	45	31	22	11	4	2	1	0	0
TPC (N = 48)	48	32	13	6	3	3	0	0	0	0	0	0

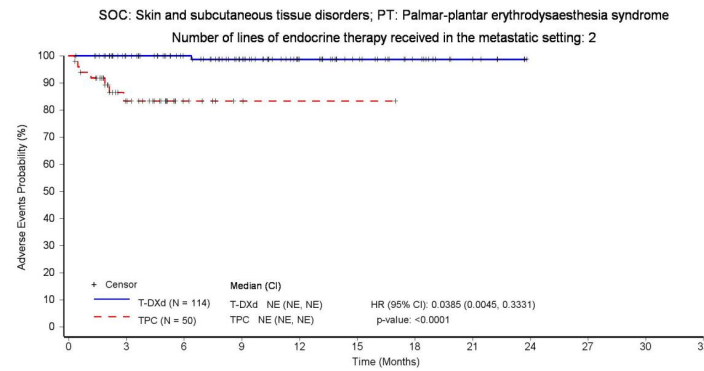
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:32; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PAT\_4\_SAS.rf

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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 114)	114	93	77	60	39	26	15	6	0	0	0	0
TPC (N = 50)	50	25	7	2	1	1	0	0	0	0	0	0

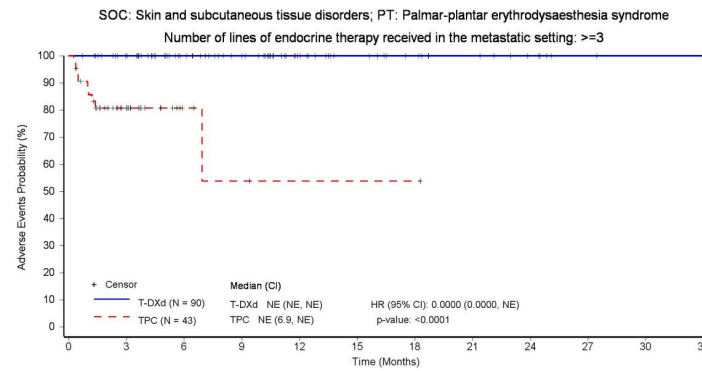
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:32; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PAT\_4\_SAS.rf

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 90)	90	81	60	45	28	20	14	10	6	2	1	0
TPC (N = 43)	43	18	4	2	1	1	1	0	0	0	0	0

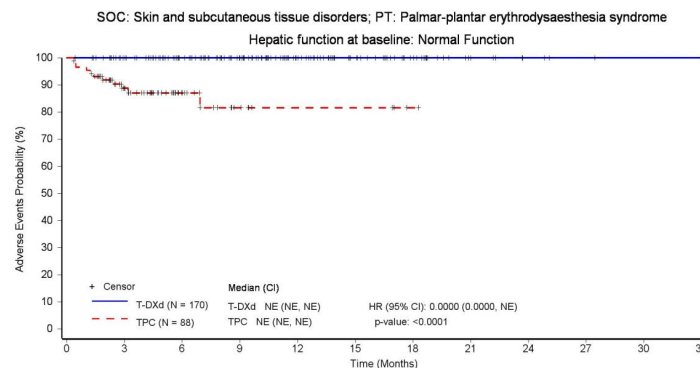
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:32; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PAT\_4\_SAS.rf

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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 170)	170	155	126	99	62	40	22	8	4	2	1	0
TPC (N = 88)	88	54	21	8	4	4	1	0	0	0	0	0

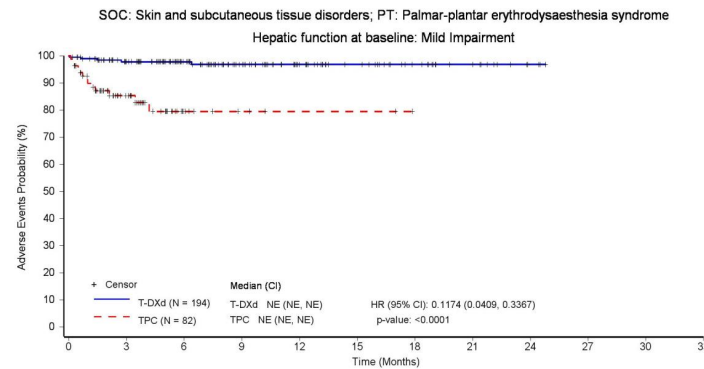
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:32; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PAT\_4\_SAS.rf

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DE.F.4.8.4 - Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 194)	194	152	107	71	47	32	21	11	3	0	0	0
TPC (N = 82)	82	38	10	4	2	2	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:32; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESOCPT10PAT\_4\_SAS.rf

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DE.T.4.9.1 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Time-to-event analysis -  
 Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Infections and infestations; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	29 (7.8)	2 (1.2)	
Number of subjects censored, n (%)	342 (92.2)	170 (98.8)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			4.6110 [1.0835, 19.6227] 0.0386
Stratified log-rank p-value [c]			0.0234

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 18:39; Program name: T4\_AESOCPT10PAT\_1\_SAS.sas; Output name: T4\_SAESOCPT5PER\_1\_SAS.rtf

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DE.T.4.9.1 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Time-to-event analysis -  
 Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	25 (6.7)	4 (2.3)	
Number of subjects censored, n (%)	346 (93.3)	168 (97.7)	
Median time to first event (months) [a] 95% Confidence Interval	NE [24.4, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.7168 [0.5823, 5.0613] 0.3272
Stratified log-rank p-value [c]			0.3221

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 18:39; Program name: T4\_AESOCPT10PAT\_1\_SAS.sas; Output name: T4\_SAESOCPT5PER\_1\_SAS.rtf

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DE.T.4.9.1 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Time-to-event analysis -  
 Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Injury, poisoning and procedural complications; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	7 (1.9)	11 (6.4)	
Number of subjects censored, n (%)	364 (98.1)	161 (93.6)	
Median time to first event (months) [a]	NE	NE	
95% Confidence Interval	[NE, NE]	[NE, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.1520
95% Confidence Interval			[0.0543, 0.4258]
p-value			0.0003
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.9.2 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.8753
HER2 IHC 1+	214	13 (6.1)	201 (93.9)	NE (NE, NE)	100	1 (1.0)	99 (99.0)	NE (NE, NE)	3.7277 (0.4808, 28.9038) 0.2080	0.1773	
HER2 IHC 2+/ISH Negative	157	16 (10.2)	141 (89.8)	NE (23.5, NE)	72	1 (1.4)	71 (98.6)	NE (NE, NE)	4.4007 (0.5731, 33.7931) 0.1543	0.1201	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.9.2 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.9981
1	220	15 (6.8)	205 (93.2)	NE (NE, NE)	94	1 (1.1)	93 (98.9)	NE (NE, NE)	3.8832 (0.5065, 29.7733) 0.1918	0.1600
>=2	150	14 (9.3)	136 (90.7)	NE (23.5, NE)	78	1 (1.3)	77 (98.7)	NE (NE, NE)	4.3663 (0.5610, 33.9836) 0.1592	0.1252

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.9999
Yes	233	16 (6.9)	217 (93.1)	NE (NE, NE)	112	0	112 (100)	NE (NE, NE)	NE (NE, NE) 0.9928	0.0390	
No	98	7 (7.1)	91 (92.9)	NE (23.5, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9954	0.1945	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.9.2 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7120
<65	289	21 (7.3)	268 (92.7)	NE (NE, NE)	126	1 (0.8)	125 (99.2)	NE (NE, NE)	5.9028 (0.7847, 44.4043) 0.0846	0.0506	
>=65	82	8 (9.8)	74 (90.2)	NE (NE, NE)	46	1 (2.2)	45 (97.8)	NE (NE, NE)	2.4655 (0.3036, 20.0216) 0.3984	0.3830	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.9.2 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1468
<75	357	28 (7.8)	329 (92.2)	NE (NE, NE)	163	1 (0.6)	162 (99.4)	NE (NE, NE)	7.7728 (1.0474, 57.6801) 0.0449	0.0179	
>=75	14	1 (7.1)	13 (92.9)	NE (8.8, NE)	9	1 (11.1)	8 (88.9)	NE (4.7, NE)	0.5000 (0.0313, 7.9940) 0.6241	0.6171	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.9362
White	175	15 (8.6)	160 (91.4)	NE (NE, NE)	85	1 (1.2)	84 (98.8)	NE (NE, NE)	4.3619 (0.5689, 33.4420) 0.1564	0.1223	
Non-White	196	14 (7.1)	182 (92.9)	NE (23.5, NE)	86	1 (1.2)	85 (98.8)	NE (NE, NE)	3.7155 (0.4778, 28.8934) 0.2098	0.1793	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.4790
Asia	147	8 (5.4)	139 (94.6)	NE (23.5, NE)	63	1 (1.6)	62 (98.4)	NE (NE, NE)	1.6399 (0.1945, 13.8279) 0.6493	0.6462	
North America	58	8 (13.8)	50 (86.2)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9944	0.1023	
Europe + Israel	166	13 (7.8)	153 (92.2)	NE (NE, NE)	81	1 (1.2)	80 (98.8)	NE (NE, NE)	4.0831 (0.5257, 31.7140) 0.1786	0.1458	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											
0	199	8 (4.0)	191 (96.0)	NE (NE, NE)	95	1 (1.1)	94 (98.9)	NE (NE, NE)	1.9699 (0.2401, 16.1604) 0.5278	0.5203	0.5058
1	172	21 (12.2)	151 (87.8)	NE (23.5, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	6.0507 (0.8026, 45.6154) 0.0807	0.0469	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1523
0	60	6 (10.0)	54 (90.0)	NE (NE, NE)	31	2 (6.5)	29 (93.5)	NE (NE, NE)	0.8939 (0.1738, 4.5978) 0.8932	0.8932	
1	107	6 (5.6)	101 (94.4)	NE (NE, NE)	48	0	48 (100)	NE (NE, NE)	NE (NE, NE) 0.9948	0.1189	
2	114	13 (11.4)	101 (88.6)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	NE (NE, NE) 0.9939	0.0888	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	4 (4.4)	86 (95.6)	NE (23.5, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9957	0.4319	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.9.2 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.8206
PD	173	12 (6.9)	161 (93.1)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	3.1702 (0.4031, 24.9331)	0.2475	
PR	48	2 (4.2)	46 (95.8)	23.5 (NE, NE)	21	0	21 (100)	NE (NE, NE)	0.2729 (NE, NE)	0.7477	
SD	82	5 (6.1)	77 (93.9)	NE (NE, NE)	54	1 (1.9)	53 (98.1)	NE (NE, NE)	2.4625 (0.2833, 21.4081)	0.3989	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.0462
Yes	37	1 (2.7)	36 (97.3)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	0.2265 (0.0134, 3.8135)	0.2626	
No	334	28 (8.4)	306 (91.6)	NE (NE, NE)	159	1 (0.6)	158 (99.4)	NE (NE, NE)	0.3026 (1.0782, 59.3232)	0.0159	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0101
Yes	24	0	24 (100)	NE (NE, NE)	7	1 (14.3)	6 (85.7)	NE (0.8, NE)	0.0000 (0.0000, ) 0.9982	0.0699	
No	347	29 (8.4)	318 (91.6)	NE (NE, NE)	165	1 (0.6)	164 (99.4)	NE (NE, NE)	8.1246 (1.0970, 60.1752) 0.0403	0.0148	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.5250
Normal Function	201	17 (8.5)	184 (91.5)	NE (NE, NE)	80	1 (1.3)	79 (98.8)	NE (NE, NE)	3.8944 (0.5087, 29.8130) 0.1905	0.1587	
Mild Impairment	123	7 (5.7)	116 (94.3)	NE (23.5, NE)	65	1 (1.5)	64 (98.5)	NE (NE, NE)	1.8823 (0.2173, 16.3062) 0.5658	0.5598	
Moderate Impairment	41	4 (9.8)	37 (90.2)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9955	0.1594	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1444
Normal Function	170	14 (8.2)	156 (91.8)	NE (23.5, NE)	88	2 (2.3)	86 (97.7)	NE (NE, NE)	1.5641 (0.3451, 7.0897) 0.5619	0.5591	
Mild Impairment	194	13 (6.7)	181 (93.3)	NE (NE, NE)	82	0	82 (100)	NE (NE, NE)	NE (NE, NE) 0.9929	0.0424	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.4971
Yes	331	26 (7.9)	305 (92.1)	NE (NE, NE)	146	2 (1.4)	144 (98.6)	NE (NE, NE)	3.6420 (0.8539, 15.5334) 0.0807	0.0619	
No	40	3 (7.5)	37 (92.5)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9972	0.4398	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.0138
Positive	329	23 (7.0)	306 (93.0)	NE (NE, NE)	152	0	152 (100)	NE (NE, NE)	NE (NE, NE) 0.9867	0.0159	
Negative	42	6 (14.3)	36 (85.7)	NE (NE, NE)	20	2 (10.0)	18 (90.0)	NE (4.7, NE)	1.0708 (0.2048, 5.5995) 0.9354	0.9387	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.0065
Positive	331	24 (7.3)	307 (92.7)	NE (NE, NE)	155	0	155 (100)	NE (NE, NE)	NE (NE, NE) 0.9911	0.0116	
Negative	40	5 (12.5)	35 (87.5)	NE (NE, NE)	17	2 (11.8)	15 (88.2)	NE (4.7, NE)	0.6843 (0.1211, 3.8673) 0.6677	0.6660	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.9290
HER2 IHC 1+	214	13 (6.1)	201 (93.9)	NE (NE, NE)	100	2 (2.0)	98 (98.0)	NE (NE, NE)	2.0005 (0.4444, 9.0052) 0.3664	0.3571	
HER2 IHC 2+/ISH Negative	157	12 (7.6)	145 (92.4)	NE (24.4, NE)	72	2 (2.8)	70 (97.2)	NE (NE, NE)	1.4963 (0.3265, 6.8572) 0.6039	0.6010	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.3667
1	220	7 (3.2)	213 (96.8)	NE (24.4, NE)	94	2 (2.1)	92 (97.9)	NE (NE, NE)	0.9165 (0.1835, 4.5764) 0.9153	0.9153	
>=2	150	18 (12.0)	132 (88.0)	NE (NE, NE)	78	2 (2.6)	76 (97.4)	NE (NE, NE)	2.6555 (0.6053, 11.6503) 0.1955	0.1788	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.9.2 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.1153
Yes	233	14 (6.0)	219 (94.0)	NE (24.4, NE)	112	4 (3.6)	108 (96.4)	NE (NE, NE)	0.9347 (0.3006, 2.9061) 0.9071	0.9066	
No	98	6 (6.1)	92 (93.9)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9954	0.1809	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4221
<65	289	20 (6.9)	269 (93.1)	NE (24.4, NE)	126	2 (1.6)	124 (98.4)	NE (NE, NE)	2.4169 (0.5562, 10.5029) 0.2391	0.2244	
>=65	82	5 (6.1)	77 (93.9)	NE (NE, NE)	46	2 (4.3)	44 (95.7)	NE (NE, NE)	1.0782 (0.2066, 5.6261) 0.9288	0.9288	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9998
<75	357	25 (7.0)	332 (93.0)	NE (24.4, NE)	163	4 (2.5)	159 (97.5)	NE (NE, NE)	1.6986 (0.5824, 4.9540) 0.3320	0.3265	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.3963
White	175	13 (7.4)	162 (92.6)	24.4 (24.4, NE)	85	3 (3.5)	82 (96.5)	NE (NE, NE)	1.2934 (0.3596, 4.6523) 0.6936	0.6928	
Non-White	196	12 (6.1)	184 (93.9)	NE (NE, NE)	86	1 (1.2)	85 (98.8)	NE (NE, NE)	3.1323 (0.4026, 24.3717) 0.2754	0.2501	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.8462
Asia	147	10 (6.8)	137 (93.2)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (NE, NE)	2.3380 (0.2944, 18.5706) 0.4218	0.4084	
North America	58	7 (12.1)	51 (87.9)	NE (NE, NE)	28	1 (3.6)	27 (96.4)	NE (NE, NE)	1.9613 (0.2330, 16.5065) 0.5354	0.5279	
Europe + Israel	166	8 (4.8)	158 (95.2)	24.4 (24.4, NE)	81	2 (2.5)	79 (97.5)	NE (NE, NE)	1.3184 (0.2720, 6.3904) 0.7314	0.7305	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.8270
0	199	8 (4.0)	191 (96.0)	NE (24.4, NE)	95	1 (1.1)	94 (98.9)	NE (NE, NE)	1.9980 (0.2425, 16.4594) 0.5200	0.5119	
1	172	17 (9.9)	155 (90.1)	NE (NE, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	1.6481 (0.4752, 5.7163) 0.4310	0.4263	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.2384
0	60	6 (10.0)	54 (90.0)	NE (18.1, NE)	31	0	31 (100)	NE (NE, NE)	NE (NE, NE) 0.9955	0.1990	
1	107	8 (7.5)	99 (92.5)	NE (NE, NE)	48	1 (2.1)	47 (97.9)	NE (NE, NE)	2.9221 (0.3643, 23.4412) 0.3128	0.2900	
2	114	7 (6.1)	107 (93.9)	NE (NE, NE)	50	1 (2.0)	49 (98.0)	NE (NE, NE)	1.7228 (0.2073, 14.3175) 0.6146	0.6104	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	4 (4.4)	86 (95.6)	NE (24.4, NE)	43	2 (4.7)	41 (95.3)	NE (NE, NE)	0.4191 (0.0649, 2.7049) 0.3607	0.3477	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.3181
PD	173	15 (8.7)	158 (91.3)	NE (24.4, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	1.9021 (0.4228, 8.5574)	0.3942	
PR	48	1 (2.1)	47 (97.9)	NE (NE, NE)	21	1 (4.8)	20 (95.2)	NE (NE, NE)	0.4345 (0.0272, 6.9496)	0.5446	
SD	82	1 (1.2)	81 (98.8)	NE (NE, NE)	54	1 (1.9)	53 (98.1)	NE (NE, NE)	0.3911 (0.0245, 6.2545)	0.4912	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.3562
Yes	37	4 (10.8)	33 (89.2)	24.4 (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9972	0.4503	
No	334	21 (6.3)	313 (93.7)	NE (NE, NE)	159	4 (2.5)	155 (97.5)	NE (NE, NE)	1.6208 (0.5502, 4.7749) 0.3810	0.3765	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.9.2 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.4040
Yes	24	3 (12.5)	21 (87.5)	24.4 (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9973	0.4565	
No	347	22 (6.3)	325 (93.7)	NE (NE, NE)	165	4 (2.4)	161 (97.6)	NE (NE, NE)	1.6146 (0.5492, 4.7467) 0.3839	0.3794	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.4666
Normal Function	201	11 (5.5)	190 (94.5)	NE (24.4, NE)	80	1 (1.3)	79 (98.8)	NE (NE, NE)	2.8848 (0.3652, 22.7905) 0.3151	0.2930	
Mild Impairment	123	11 (8.9)	112 (91.1)	NE (NE, NE)	65	3 (4.6)	62 (95.4)	NE (NE, NE)	0.9257 (0.2490, 3.4411) 0.9082	0.9072	
Moderate Impairment	41	2 (4.9)	39 (95.1)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9968	0.3253	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1668
Normal Function	170	13 (7.6)	157 (92.4)	NE (NE, NE)	88	1 (1.1)	87 (98.9)	NE (NE, NE)	4.3912 (0.5715, 33.7388) 0.1550	0.1203	
Mild Impairment	194	11 (5.7)	183 (94.3)	NE (24.4, NE)	82	3 (3.7)	79 (96.3)	NE (NE, NE)	0.8132 (0.2141, 3.0895) 0.7615	0.7611	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.3049
Yes	331	22 (6.6)	309 (93.4)	NE (24.4, NE)	146	4 (2.7)	142 (97.3)	NE (NE, NE)	1.6124 (0.5496, 4.7302) 0.3843	0.3798	
No	40	3 (7.5)	37 (92.5)	NE (18.1, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9969	0.5959	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.1192
Positive	329	18 (5.5)	311 (94.5)	NE (24.4, NE)	152	4 (2.6)	148 (97.4)	NE (NE, NE)	1.2011 (0.3980, 3.6248)	0.7447	
Negative	42	7 (16.7)	35 (83.3)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) 0.9950	0.1365	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (derived)											0.1977
Positive	331	19 (5.7)	312 (94.3)	NE (24.4, NE)	155	4 (2.6)	151 (97.4)	NE (NE, NE)	1.3679 (0.4577, 4.0883)	0.5732	
Negative	40	6 (15.0)	34 (85.0)	NE (11.1, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) 0.9962	0.2712	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0745
HER2 IHC 1+	214	3 (1.4)	211 (98.6)	NE (NE, NE)	100	9 (9.0)	91 (91.0)	NE (NE, NE)	0.0869 (0.0216, 0.3494) 0.0006	<0.0001	
HER2 IHC 2+/ISH Negative	157	4 (2.5)	153 (97.5)	NE (NE, NE)	72	2 (2.8)	70 (97.2)	NE (NE, NE)	0.5391 (0.0951, 3.0547) 0.4850	0.4787	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.0013
1	220	0	220 (100)	NE (NE, NE)	94	7 (7.4)	87 (92.6)	NE (NE, NE)	0.0000 (0.0000, ) 0.9943	<0.0001	
>=2	150	7 (4.7)	143 (95.3)	NE (NE, NE)	78	4 (5.1)	74 (94.9)	NE (NE, NE)	0.3828 (0.1060, 1.3828) 0.1428	0.1310	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.3626
Yes	233	1 (0.4)	232 (99.6)	NE (NE, NE)	112	4 (3.6)	108 (96.4)	NE (NE, NE)	0.0998 (0.0110, 0.9067) 0.0407	0.0122	
No	98	5 (5.1)	93 (94.9)	NE (NE, NE)	43	6 (14.0)	37 (86.0)	NE (NE, NE)	0.2156 (0.0636, 0.7309) 0.0138	0.0080	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5461
<65	289	4 (1.4)	285 (98.6)	NE (NE, NE)	126	7 (5.6)	119 (94.4)	NE (NE, NE)	0.1464 (0.0402, 0.5338) 0.0036	0.0011	
>=65	82	3 (3.7)	79 (96.3)	NE (NE, NE)	46	4 (8.7)	42 (91.3)	NE (NE, NE)	0.2673 (0.0570, 1.2528) 0.0941	0.0750	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4272
<75	357	6 (1.7)	351 (98.3)	NE (NE, NE)	163	10 (6.1)	153 (93.9)	NE (NE, NE)	0.1503 (0.0515, 0.4390) 0.0005	0.0001	
>=75	14	1 (7.1)	13 (92.9)	NE (5.1, NE)	9	1 (11.1)	8 (88.9)	NE (0.0, NE)	0.5071 (0.0311, 8.2671) 0.6335	0.6272	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.1405
White	175	1 (0.6)	174 (99.4)	NE (NE, NE)	85	0	85 (100)	NE (NE, NE)	NE (NE, NE) 0.9982	0.6291	
Non-White	196	6 (3.1)	190 (96.9)	NE (NE, NE)	86	11 (12.8)	75 (87.2)	NE (NE, NE)	0.1371 (0.0484, 0.3879) 0.0002	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.6697
Asia	147	4 (2.7)	143 (97.3)	NE (NE, NE)	63	8 (12.7)	55 (87.3)	NE (NE, NE)	0.1315 (0.0376, 0.4600) 0.0015	0.0003	
North America	58	1 (1.7)	57 (98.3)	NE (NE, NE)	28	1 (3.6)	27 (96.4)	NE (NE, NE)	0.3023 (0.0185, 4.9348) 0.4012	0.3742	
Europe + Israel	166	2 (1.2)	164 (98.8)	NE (NE, NE)	81	2 (2.5)	79 (97.5)	NE (NE, NE)	0.2170 (0.0285, 1.6510) 0.1400	0.1100	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.0118
0	199	1 (0.5)	198 (99.5)	NE (NE, NE)	95	8 (8.4)	87 (91.6)	NE (NE, NE)	0.0458 (0.0056, 0.3714) 0.0039	<0.0001	
1	172	6 (3.5)	166 (96.5)	NE (NE, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	0.3921 (0.0889, 1.7297) 0.2163	0.2035	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.0150
0	60	3 (5.0)	57 (95.0)	NE (NE, NE)	31	3 (9.7)	28 (90.3)	NE (NE, NE)	0.2637 (0.0478, 1.4534) 0.1259	0.1082	
1	107	1 (0.9)	106 (99.1)	NE (NE, NE)	48	5 (10.4)	43 (89.6)	NE (NE, NE)	0.0730 (0.0084, 0.6361) 0.0178	0.0023	
2	114	0	114 (100)	NE (NE, NE)	50	3 (6.0)	47 (94.0)	NE (NE, NE)	0.0000 (0.0000, ) 0.9967	0.0021	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	3 (3.3)	87 (96.7)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9960	0.5040	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.2910
PD	173	4 (2.3)	169 (97.7)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	0.8345 (0.0875, 7.9541)	0.8749	
PR	48	2 (4.2)	46 (95.8)	NE (16.5, NE)	21	3 (14.3)	18 (85.7)	NE (5.5, NE)	0.0506 (0.0043, 0.5894)	0.0030	
SD	82	1 (1.2)	81 (98.8)	NE (NE, NE)	54	2 (3.7)	52 (96.3)	NE (NE, NE)	0.2673 (0.0238, 3.0070)	0.2541	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.1846
Yes	37	1 (2.7)	36 (97.3)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9985	0.7055	
No	334	6 (1.8)	328 (98.2)	NE (NE, NE)	159	11 (6.9)	148 (93.1)	NE (NE, NE)	0.1491 (0.0523, 0.4245) 0.0004	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.1781
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9982	0.6374	
No	347	6 (1.7)	341 (98.3)	NE (NE, NE)	165	11 (6.7)	154 (93.3)	NE (NE, NE)	0.1469 (0.0515, 0.4188) 0.0003	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.3465
Normal Function	201	2 (1.0)	199 (99.0)	NE (NE, NE)	80	3 (3.8)	77 (96.3)	NE (NE, NE)	0.1543 (0.0228, 1.0457) 0.0556	0.0316	
Mild Impairment	123	3 (2.4)	120 (97.6)	NE (NE, NE)	65	7 (10.8)	58 (89.2)	NE (NE, NE)	0.1389 (0.0344, 0.5617) 0.0056	0.0016	
Moderate Impairment	41	2 (4.9)	39 (95.1)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	0.8564 (0.0768, 9.5473) 0.8997	0.8996	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1859
Normal Function	170	5 (2.9)	165 (97.1)	NE (NE, NE)	88	5 (5.7)	83 (94.3)	NE (NE, NE)	0.3005 (0.0833, 1.0838) 0.0662	0.0541	
Mild Impairment	194	2 (1.0)	192 (99.0)	NE (NE, NE)	82	6 (7.3)	76 (92.7)	NE (NE, NE)	0.0796 (0.0144, 0.4381) 0.0036	0.0004	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 18:39; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_SAESOCPT5PER\_2\_SAS.rtf

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DE.T.4.9.2 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.8594
Yes	331	6 (1.8)	325 (98.2)	NE (NE, NE)	146	9 (6.2)	137 (93.8)	NE (NE, NE)	0.1851 (0.0638, 0.5373) 0.0019	0.0006	
No	40	1 (2.5)	39 (97.5)	NE (NE, NE)	26	2 (7.7)	24 (92.3)	NE (NE, NE)	0.1199 (0.0071, 2.0122) 0.1405	0.1079	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 18:39; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_SAESOCPT5PER\_2\_SAS.rtf

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DE.T.4.9.2 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.7587
Positive	329	6 (1.8)	323 (98.2)	NE (NE, NE)	152	10 (6.6)	142 (93.4)	NE (NE, NE)	0.1618 (0.0562, 0.4658)	0.0002	
Negative	42	1 (2.4)	41 (97.6)	NE (NE, NE)	20	1 (5.0)	19 (95.0)	NE (NE, NE)	0.2865 (0.0164, 5.0118)	0.3658	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 18:39; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_SAESOCPT5PER\_2\_SAS.rtf

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DE.T.4.9.2 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.8468
Positive	331	6 (1.8)	325 (98.2)	NE (NE, NE)	155	10 (6.5)	145 (93.5)	NE (NE, NE)	0.1635 (0.0567, 0.4712)	0.0002	
Negative	40	1 (2.5)	39 (97.5)	NE (NE, NE)	17	1 (5.9)	16 (94.1)	NE (NE, NE)	0.2062 (0.0107, 3.9591)	0.2583	

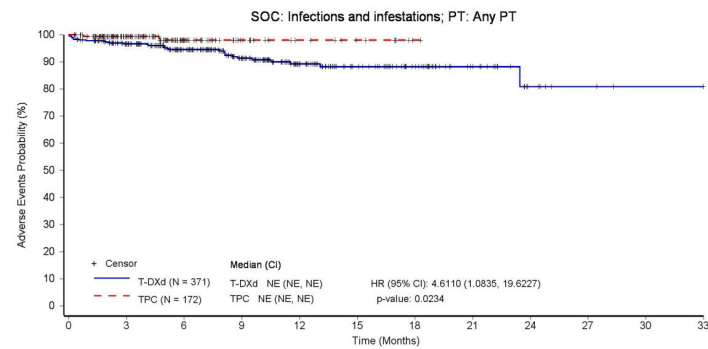
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Run date: 13SEP2022 – 18:39; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_SAESOCPT5PER\_2\_SAS.rtf

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DE.F.4.9.3 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

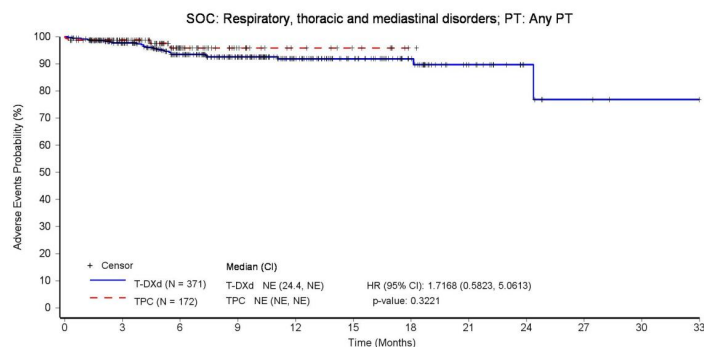
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	309	230	163	100	66	42	20	7	3	1	0
TPC (N = 172)	172	107	43	20	11	7	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	311	231	171	108	72	43	19	7	3	1	0
TPC (N = 172)	172	106	44	20	11	7	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

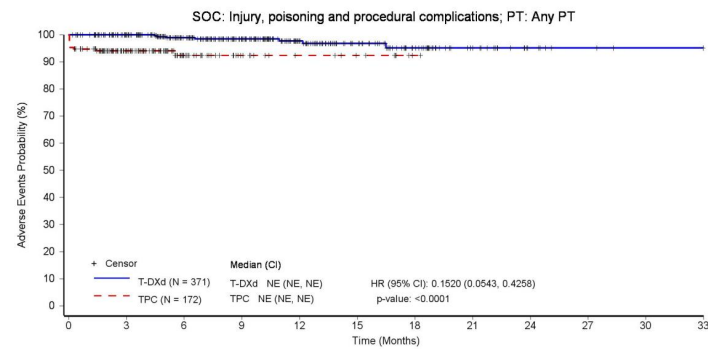
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DE.F.4.9.3 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	314	236	174	110	72	43	19	7	3	1	0
TPC (N = 172)	172	172	100	38	17	10	7	1	0	0	0	0

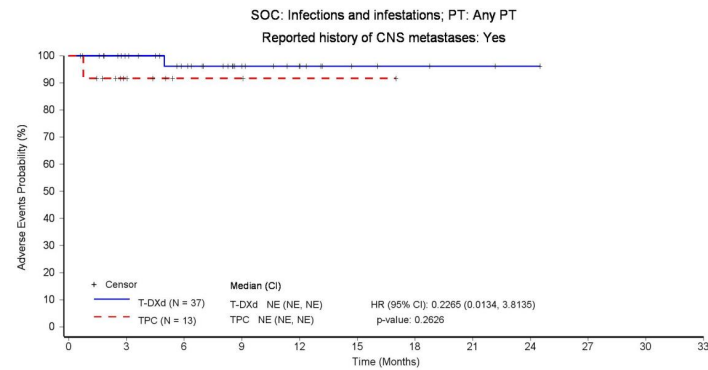
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.9.4 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 37)	37	30	23	14	9	4	3	2	1	0	0	0
TPC (N = 13)	13	6	2	2	1	1	0	0	0	0	0	0

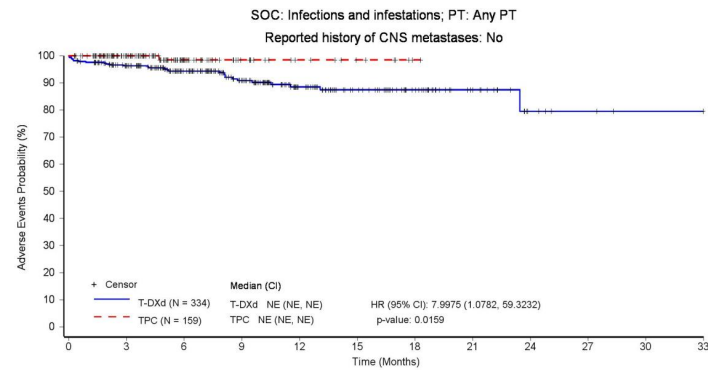
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.9.4 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

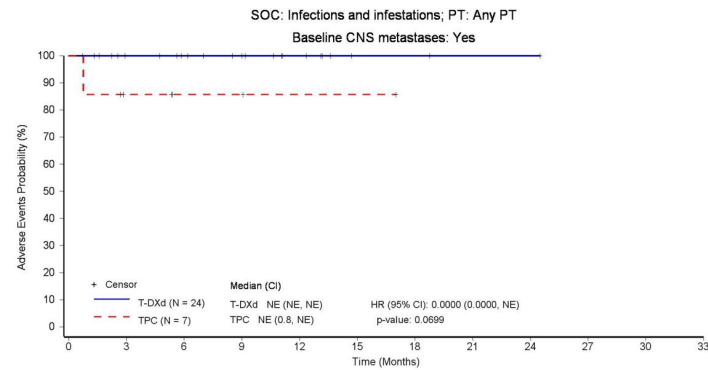
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 334)	334	279	207	149	91	62	39	18	6	3	1	0
TPC (N = 159)	159	101	41	18	10	6	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 24)	24	18	15	12	7	2	2	1	1	0	0	0
TPC (N = 7)	7	4	2	2	1	1	0	0	0	0	0	0

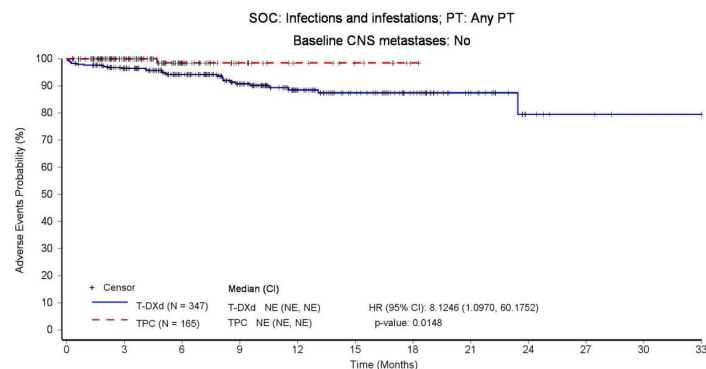
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.9.4 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 347)	347	291	215	151	93	64	40	19	6	3	1	0
TPC (N = 165)	165	103	41	18	10	6	1	0	0	0	0	0

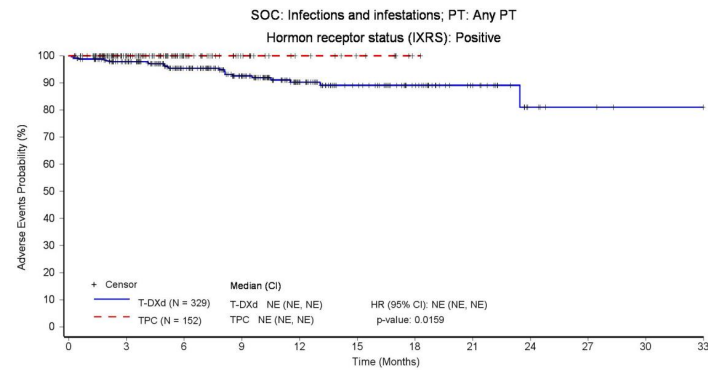
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 329)	329	280	210	150	92	61	38	19	6	3	1	0
TPC (N = 152)	152	95	41	20	11	7	1	0	0	0	0	0

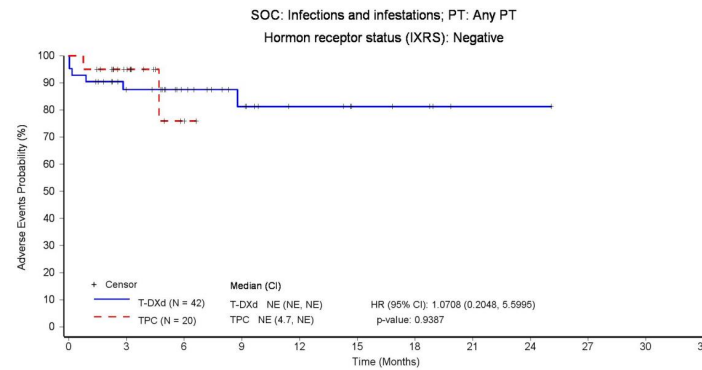
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

T-DXd (N = 42)	42	29	20	13	8	5	4	1	1	0	0	0
TPC (N = 20)	20	12	2	0	0	0	0	0	0	0	0	0

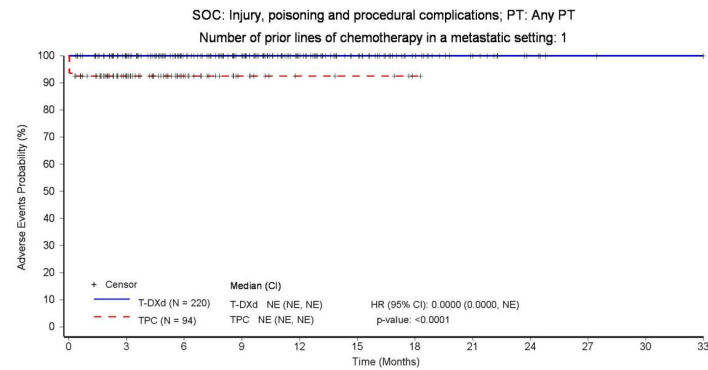
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 220)	220	186	139	108	69	45	23	12	5	2	1	0
TPC (N = 94)	94	56	25	11	5	4	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

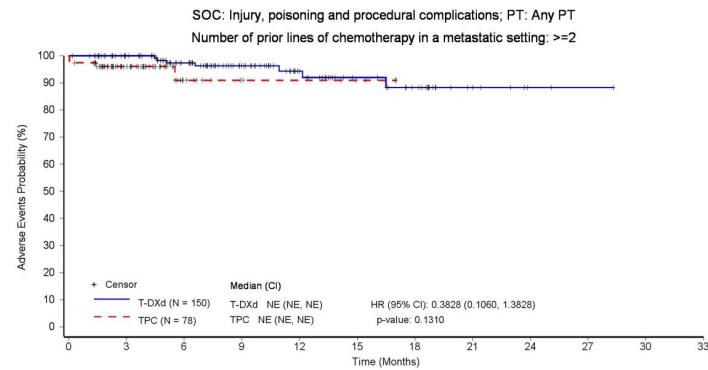
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 150)	150	127	96	65	40	26	19	6	2	1	0	0
TPC (N = 78)	78	44	13	6	5	3	0	0	0	0	0	0

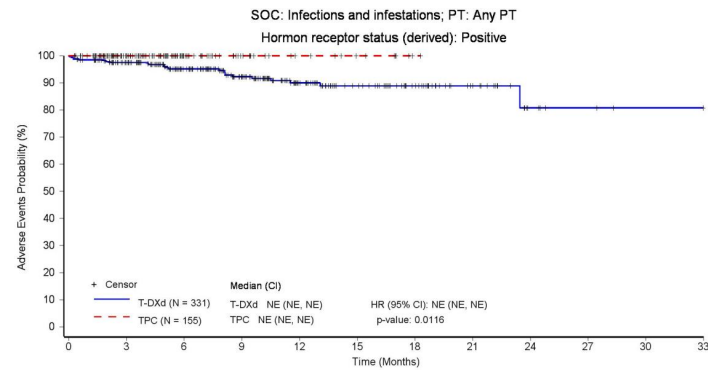
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:53; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_SAESOCPT5PER\_4\_SAS.rtf

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DE.F.4.9.4 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 331)	331	280	210	151	93	62	39	19	6	3	1	0
TPC (N = 155)	155	98	41	20	11	7	1	0	0	0	0	0

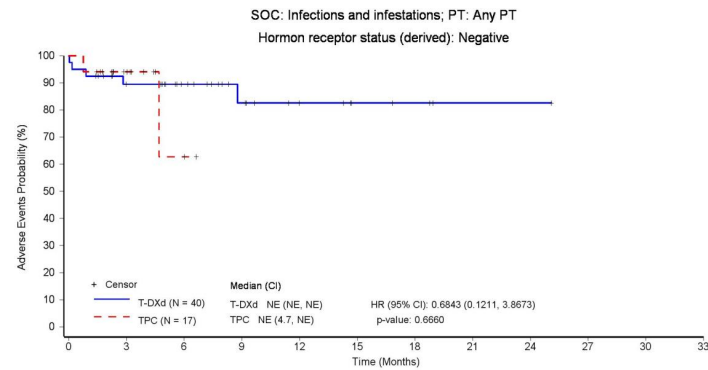
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:53; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_SAESOCPT5PER\_4\_SAS.rtf

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DE.F.4.9.4 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 40)	40	29	20	12	7	4	3	1	1	0	0	0
TPC (N = 17)	17	9	2	0	0	0	0	0	0	0	0	0

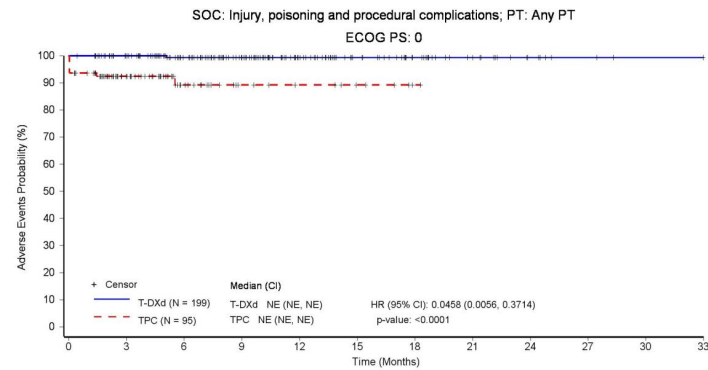
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:53; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_SAESOCPT5PER\_4\_SAS.rtf

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DE.F.4.9.4 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 199)	199	178	138	106	67	45	28	15	7	3	1	0
TPC (N = 95)	95	54	24	11	8	5	1	0	0	0	0	0

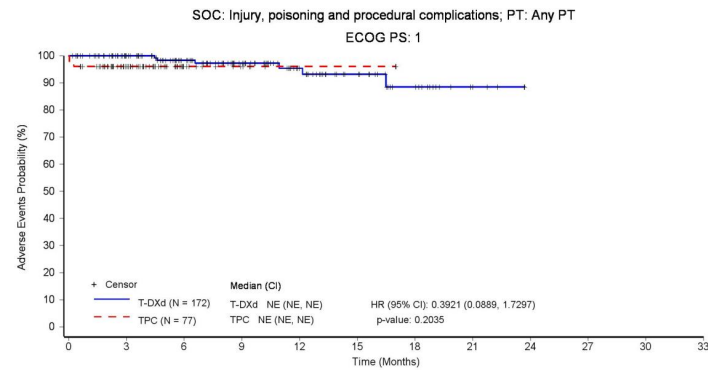
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:53; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_SAESOCPT5PER\_4\_SAS.rtf

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DE.F.4.9.4 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 172)	172	136	98	68	43	27	15	4	0	0	0	0
TPC (N = 77)	77	46	14	6	2	2	0	0	0	0	0	0

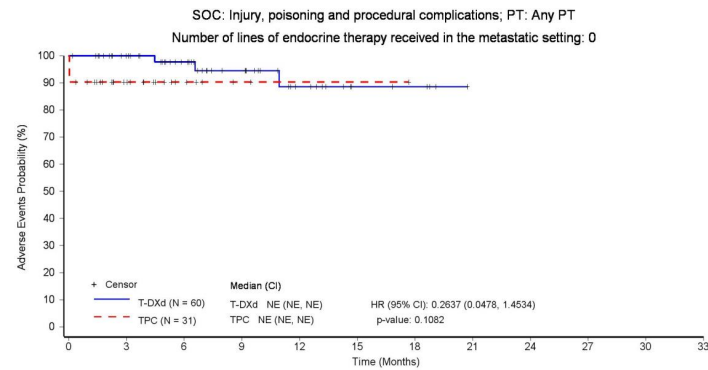
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:53; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_SAESOCPT5PER\_4\_SAS.rtf

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DE.F.4.9.4 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 60)	60	49	34	23	12	5	4	0	0	0	0	0
TPC (N = 31)	31	16	6	2	1	1	0	0	0	0	0	0

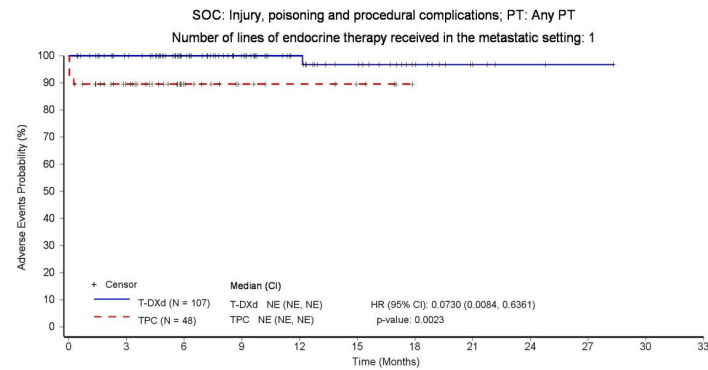
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:53; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_SAESOCPT5PER\_4\_SAS.rtf

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DE.F.4.9.4 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 107)	107	91	67	47	31	21	11	4	2	1	0	0
TPC (N = 48)	48	32	15	8	6	4	0	0	0	0	0	0

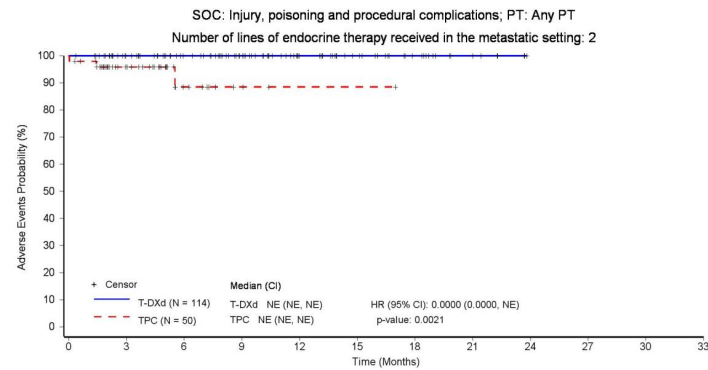
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:53; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_SAESOCPT5PER\_4\_SAS.rtf

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DE.F.4.9.4 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 114)	114	93	77	60	39	26	15	6	0	0	0	0
TPC (N = 50)	50	29	9	3	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

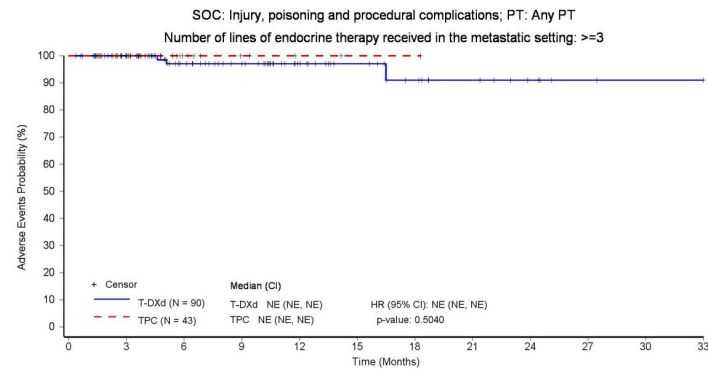
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DE.F.4.9.4 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

T-DXd (N = 90)	90	81	58	44	28	20	13	9	5	2	1	0
TPC (N = 43)	43	23	8	4	2	1	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:53; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_SAESOCPT5PER\_4\_SAS.rtf

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DE.T.4.10.1 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Infections and infestations; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	29 (7.8)	2 (1.2)	
Number of subjects censored, n (%)	342 (92.2)	170 (98.8)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			4.6110 [1.0835, 19.6227] 0.0386
Stratified log-rank p-value [c]			0.0234

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 18:42; Program name: T4\_AESOCPT10PAT\_1\_SAS.sas; Output name: T4\_SAESOCPT10PAT\_1\_SAS.rtf

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DE.T.4.10.1 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	25 (6.7)	4 (2.3)	
Number of subjects censored, n (%)	346 (93.3)	168 (97.7)	
Median time to first event (months) [a] 95% Confidence Interval	NE [24.4, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.7168 [0.5823, 5.0613] 0.3272
Stratified log-rank p-value [c]			0.3221

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 18:42; Program name: T4\_AESOCPT10PAT\_1\_SAS.sas; Output name: T4\_SAESOCPT10PAT\_1\_SAS.rtf

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DE.T.4.10.1 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Gastrointestinal disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	18 (4.9)	3 (1.7)	
Number of subjects censored, n (%)	353 (95.1)	169 (98.3)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			2.0577 [0.5953, 7.1120] 0.2541
Stratified log-rank p-value [c]			0.2441

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 18:42; Program name: T4\_AESOCPT10PAT\_1\_SAS.sas; Output name: T4\_SAESOCPT10PAT\_1\_SAS.rtf

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DE.T.4.10.1 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: General disorders and administration site conditions; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	16 (4.3)	3 (1.7)	
Number of subjects censored, n (%)	355 (95.7)	169 (98.3)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.5474 [0.4380, 5.4666] 0.4978
Stratified log-rank p-value [c]			0.4946

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 18:42; Program name: T4\_AESOCPT10PAT\_1\_SAS.sas; Output name: T4\_SAESOCPT10PAT\_1\_SAS.rtf

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DE.T.4.10.1 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for &gt;= 10 patients in at least one arm and &gt;= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

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SOC: Injury, poisoning and procedural complications; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	7 (1.9)	11 (6.4)	
Number of subjects censored, n (%)	364 (98.1)	161 (93.6)	
Median time to first event (months) [a]	NE	NE	
95% Confidence Interval	[NE, NE]	[NE, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.1520
95% Confidence Interval			[0.0543, 0.4258]
p-value			0.0003
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 13SEP2022 – 18:42; Program name: T4\_AESOCPT10PAT\_1\_SAS.sas; Output name: T4\_SAESOCPT10PAT\_1\_SAS.rtf

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DE.T.4.10.2 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.8753
HER2 IHC 1+	214	13 (6.1)	201 (93.9)	NE (NE, NE)	100	1 (1.0)	99 (99.0)	NE (NE, NE)	3.7277 (0.4808, 28.9038) 0.2080	0.1773
HER2 IHC 2+/ISH Negative	157	16 (10.2)	141 (89.8)	NE (23.5, NE)	72	1 (1.4)	71 (98.6)	NE (NE, NE)	4.4007 (0.5731, 33.7931) 0.1543	0.1201

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 18:42; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_SAESOCPT10PAT\_2\_SAS.rtf

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DE.T.4.10.2 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Number of prior lines of chemotherapy in a metastatic setting										0.9981
1	220	15 (6.8)	205 (93.2)	NE (NE, NE)	94	1 (1.1)	93 (98.9)	NE (NE, NE)	3.8832 (0.5065, 29.7733) 0.1918	0.1600
>=2	150	14 (9.3)	136 (90.7)	NE (23.5, NE)	78	1 (1.3)	77 (98.7)	NE (NE, NE)	4.3663 (0.5610, 33.9836) 0.1592	0.1252

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.9999
Yes	233	16 (6.9)	217 (93.1)	NE (NE, NE)	112	0	112 (100)	NE (NE, NE)	NE (NE, NE) 0.9928	0.0390	
No	98	7 (7.1)	91 (92.9)	NE (23.5, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9954	0.1945	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7120
<65	289	21 (7.3)	268 (92.7)	NE (NE, NE)	126	1 (0.8)	125 (99.2)	NE (NE, NE)	5.9028 (0.7847, 44.4043) 0.0846	0.0506	
>=65	82	8 (9.8)	74 (90.2)	NE (NE, NE)	46	1 (2.2)	45 (97.8)	NE (NE, NE)	2.4655 (0.3036, 20.0216) 0.3984	0.3830	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1468
<75	357	28 (7.8)	329 (92.2)	NE (NE, NE)	163	1 (0.6)	162 (99.4)	NE (NE, NE)	7.7728 (1.0474, 57.6801) 0.0449	0.0179	
>=75	14	1 (7.1)	13 (92.9)	NE (8.8, NE)	9	1 (11.1)	8 (88.9)	NE (4.7, NE)	0.5000 (0.0313, 7.9940) 0.6241	0.6171	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.9362
White	175	15 (8.6)	160 (91.4)	NE (NE, NE)	85	1 (1.2)	84 (98.8)	NE (NE, NE)	4.3619 (0.5689, 33.4420) 0.1564	0.1223	
Non-White	196	14 (7.1)	182 (92.9)	NE (23.5, NE)	86	1 (1.2)	85 (98.8)	NE (NE, NE)	3.7155 (0.4778, 28.8934) 0.2098	0.1793	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.4790
Asia	147	8 (5.4)	139 (94.6)	NE (23.5, NE)	63	1 (1.6)	62 (98.4)	NE (NE, NE)	1.6399 (0.1945, 13.8279) 0.6493	0.6462	
North America	58	8 (13.8)	50 (86.2)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9944	0.1023	
Europe + Israel	166	13 (7.8)	153 (92.2)	NE (NE, NE)	81	1 (1.2)	80 (98.8)	NE (NE, NE)	4.0831 (0.5257, 31.7140) 0.1786	0.1458	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.5058
0	199	8 (4.0)	191 (96.0)	NE (NE, NE)	95	1 (1.1)	94 (98.9)	NE (NE, NE)	1.9699 (0.2401, 16.1604) 0.5278	0.5203	
1	172	21 (12.2)	151 (87.8)	NE (23.5, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	6.0507 (0.8026, 45.6154) 0.0807	0.0469	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1523
0	60	6 (10.0)	54 (90.0)	NE (NE, NE)	31	2 (6.5)	29 (93.5)	NE (NE, NE)	0.8939 (0.1738, 4.5978) 0.8932	0.8932	
1	107	6 (5.6)	101 (94.4)	NE (NE, NE)	48	0	48 (100)	NE (NE, NE)	NE (NE, NE) 0.9948	0.1189	
2	114	13 (11.4)	101 (88.6)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	NE (NE, NE) 0.9939	0.0888	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	4 (4.4)	86 (95.6)	NE (23.5, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9957	0.4319	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.8206
PD	173	12 (6.9)	161 (93.1)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	3.1702 (0.4031, 24.9331)	0.2475	
PR	48	2 (4.2)	46 (95.8)	23.5 (NE, NE)	21	0	21 (100)	NE (NE, NE)	0.2729 (NE, NE)	0.7477	
SD	82	5 (6.1)	77 (93.9)	NE (NE, NE)	54	1 (1.9)	53 (98.1)	NE (NE, NE)	2.4625 (0.2833, 21.4081)	0.3989	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Reported history of CNS metastases											0.0462
Yes	37	1 (2.7)	36 (97.3)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	0.2265 (0.0134, 3.8135)	0.2626	
No	334	28 (8.4)	306 (91.6)	NE (NE, NE)	159	1 (0.6)	158 (99.4)	NE (NE, NE)	0.3026 (1.0782, 59.3232)	0.0159	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0101
Yes	24	0	24 (100)	NE (NE, NE)	7	1 (14.3)	6 (85.7)	NE (0.8, NE)	0.0000 (0.0000, ) 0.9982	0.0699	
No	347	29 (8.4)	318 (91.6)	NE (NE, NE)	165	1 (0.6)	164 (99.4)	NE (NE, NE)	8.1246 (1.0970, 60.1752) 0.0403	0.0148	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.5250
Normal Function	201	17 (8.5)	184 (91.5)	NE (NE, NE)	80	1 (1.3)	79 (98.8)	NE (NE, NE)	3.8944 (0.5087, 29.8130) 0.1905	0.1587	
Mild Impairment	123	7 (5.7)	116 (94.3)	NE (23.5, NE)	65	1 (1.5)	64 (98.5)	NE (NE, NE)	1.8823 (0.2173, 16.3062) 0.5658	0.5598	
Moderate Impairment	41	4 (9.8)	37 (90.2)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9955	0.1594	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1444
Normal Function	170	14 (8.2)	156 (91.8)	NE (23.5, NE)	88	2 (2.3)	86 (97.7)	NE (NE, NE)	1.5641 (0.3451, 7.0897) 0.5619	0.5591	
Mild Impairment	194	13 (6.7)	181 (93.3)	NE (NE, NE)	82	0	82 (100)	NE (NE, NE)	NE (NE, NE) 0.9929	0.0424	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.4971
Yes	331	26 (7.9)	305 (92.1)	NE (NE, NE)	146	2 (1.4)	144 (98.6)	NE (NE, NE)	3.6420 (0.8539, 15.5334) 0.0807	0.0619	
No	40	3 (7.5)	37 (92.5)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9972	0.4398	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.0138
Positive	329	23 (7.0)	306 (93.0)	NE (NE, NE)	152	0	152 (100)	NE (NE, NE)	NE (NE, NE) 0.9867	0.0159	
Negative	42	6 (14.3)	36 (85.7)	NE (NE, NE)	20	2 (10.0)	18 (90.0)	NE (4.7, NE)	1.0708 (0.2048, 5.5995) 0.9354	0.9387	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.0065
Positive	331	24 (7.3)	307 (92.7)	NE (NE, NE)	155	0	155 (100)	NE (NE, NE)	NE (NE, NE) 0.9911	0.0116	
Negative	40	5 (12.5)	35 (87.5)	NE (NE, NE)	17	2 (11.8)	15 (88.2)	NE (4.7, NE)	0.6843 (0.1211, 3.8673) 0.6677	0.6660	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.9290
HER2 IHC 1+	214	13 (6.1)	201 (93.9)	NE (NE, NE)	100	2 (2.0)	98 (98.0)	NE (NE, NE)	2.0005 (0.4444, 9.0052) 0.3664	0.3571	
HER2 IHC 2+/ISH Negative	157	12 (7.6)	145 (92.4)	NE (24.4, NE)	72	2 (2.8)	70 (97.2)	NE (NE, NE)	1.4963 (0.3265, 6.8572) 0.6039	0.6010	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.3667
1	220	7 (3.2)	213 (96.8)	NE (24.4, NE)	94	2 (2.1)	92 (97.9)	NE (NE, NE)	0.9165 (0.1835, 4.5764) 0.9153	0.9153	
>=2	150	18 (12.0)	132 (88.0)	NE (NE, NE)	78	2 (2.6)	76 (97.4)	NE (NE, NE)	2.6555 (0.6053, 11.6503) 0.1955	0.1788	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.1153
Yes	233	14 (6.0)	219 (94.0)	NE (24.4, NE)	112	4 (3.6)	108 (96.4)	NE (NE, NE)	0.9347 (0.3006, 2.9061) 0.9071	0.9066	
No	98	6 (6.1)	92 (93.9)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9954	0.1809	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4221
<65	289	20 (6.9)	269 (93.1)	NE (24.4, NE)	126	2 (1.6)	124 (98.4)	NE (NE, NE)	2.4169 (0.5562, 10.5029) 0.2391	0.2244	
>=65	82	5 (6.1)	77 (93.9)	NE (NE, NE)	46	2 (4.3)	44 (95.7)	NE (NE, NE)	1.0782 (0.2066, 5.6261) 0.9288	0.9288	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9998
<75	357	25 (7.0)	332 (93.0)	NE (24.4, NE)	163	4 (2.5)	159 (97.5)	NE (NE, NE)	1.6986 (0.5824, 4.9540) 0.3320	0.3265	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.3963
White	175	13 (7.4)	162 (92.6)	24.4 (24.4, NE)	85	3 (3.5)	82 (96.5)	NE (NE, NE)	1.2934 (0.3596, 4.6523) 0.6936	0.6928	
Non-White	196	12 (6.1)	184 (93.9)	NE (NE, NE)	86	1 (1.2)	85 (98.8)	NE (NE, NE)	3.1323 (0.4026, 24.3717) 0.2754	0.2501	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.8462
Asia	147	10 (6.8)	137 (93.2)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (NE, NE)	2.3380 (0.2944, 18.5706) 0.4218	0.4084	
North America	58	7 (12.1)	51 (87.9)	NE (NE, NE)	28	1 (3.6)	27 (96.4)	NE (NE, NE)	1.9613 (0.2330, 16.5065) 0.5354	0.5279	
Europe + Israel	166	8 (4.8)	158 (95.2)	24.4 (24.4, NE)	81	2 (2.5)	79 (97.5)	NE (NE, NE)	1.3184 (0.2720, 6.3904) 0.7314	0.7305	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.8270
0	199	8 (4.0)	191 (96.0)	NE (24.4, NE)	95	1 (1.1)	94 (98.9)	NE (NE, NE)	1.9980 (0.2425, 16.4594) 0.5200	0.5119	
1	172	17 (9.9)	155 (90.1)	NE (NE, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	1.6481 (0.4752, 5.7163) 0.4310	0.4263	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.2384
0	60	6 (10.0)	54 (90.0)	NE (18.1, NE)	31	0	31 (100)	NE (NE, NE)	NE (NE, NE) 0.9955	0.1990	
1	107	8 (7.5)	99 (92.5)	NE (NE, NE)	48	1 (2.1)	47 (97.9)	NE (NE, NE)	2.9221 (0.3643, 23.4412) 0.3128	0.2900	
2	114	7 (6.1)	107 (93.9)	NE (NE, NE)	50	1 (2.0)	49 (98.0)	NE (NE, NE)	1.7228 (0.2073, 14.3175) 0.6146	0.6104	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	4 (4.4)	86 (95.6)	NE (24.4, NE)	43	2 (4.7)	41 (95.3)	NE (NE, NE)	0.4191 (0.0649, 2.7049) 0.3607	0.3477	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.3181
PD	173	15 (8.7)	158 (91.3)	NE (24.4, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	1.9021 (0.4228, 8.5574)	0.3942	
PR	48	1 (2.1)	47 (97.9)	NE (NE, NE)	21	1 (4.8)	20 (95.2)	NE (NE, NE)	0.4345 (0.0272, 6.9496)	0.5446	
SD	82	1 (1.2)	81 (98.8)	NE (NE, NE)	54	1 (1.9)	53 (98.1)	NE (NE, NE)	0.3911 (0.0245, 6.2545)	0.4912	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.3562
Yes	37	4 (10.8)	33 (89.2)	24.4 (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9972	0.4503	
No	334	21 (6.3)	313 (93.7)	NE (NE, NE)	159	4 (2.5)	155 (97.5)	NE (NE, NE)	1.6208 (0.5502, 4.7749) 0.3810	0.3765	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.4040
Yes	24	3 (12.5)	21 (87.5)	24.4 (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9973	0.4565	
No	347	22 (6.3)	325 (93.7)	NE (NE, NE)	165	4 (2.4)	161 (97.6)	NE (NE, NE)	1.6146 (0.5492, 4.7467) 0.3839	0.3794	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.4666
Normal Function	201	11 (5.5)	190 (94.5)	NE (24.4, NE)	80	1 (1.3)	79 (98.8)	NE (NE, NE)	2.8848 (0.3652, 22.7905) 0.3151	0.2930	
Mild Impairment	123	11 (8.9)	112 (91.1)	NE (NE, NE)	65	3 (4.6)	62 (95.4)	NE (NE, NE)	0.9257 (0.2490, 3.4411) 0.9082	0.9072	
Moderate Impairment	41	2 (4.9)	39 (95.1)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9968	0.3253	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Run date: 13SEP2022 – 18:42; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_SAESOCPT10PAT\_2\_SAS.rtf

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DE.T.4.10.2 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1668
Normal Function	170	13 (7.6)	157 (92.4)	NE (NE, NE)	88	1 (1.1)	87 (98.9)	NE (NE, NE)	4.3912 (0.5715, 33.7388) 0.1550	0.1203	
Mild Impairment	194	11 (5.7)	183 (94.3)	NE (24.4, NE)	82	3 (3.7)	79 (96.3)	NE (NE, NE)	0.8132 (0.2141, 3.0895) 0.7615	0.7611	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.10.2 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.3049
Yes	331	22 (6.6)	309 (93.4)	NE (24.4, NE)	146	4 (2.7)	142 (97.3)	NE (NE, NE)	1.6124 (0.5496, 4.7302) 0.3843	0.3798	
No	40	3 (7.5)	37 (92.5)	NE (18.1, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9969	0.5959	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.1192
Positive	329	18 (5.5)	311 (94.5)	NE (24.4, NE)	152	4 (2.6)	148 (97.4)	NE (NE, NE)	1.2011 (0.3980, 3.6248)	0.7447	
Negative	42	7 (16.7)	35 (83.3)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) 0.9950	0.1365	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.1977
Positive	331	19 (5.7)	312 (94.3)	NE (24.4, NE)	155	4 (2.6)	151 (97.4)	NE (NE, NE)	1.3679 (0.4577, 4.0883)	0.5732	
Negative	40	6 (15.0)	34 (85.0)	NE (11.1, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) 0.9962	0.2712	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.8333
HER2 IHC 1+	214	13 (6.1)	201 (93.9)	NE (NE, NE)	100	2 (2.0)	98 (98.0)	NE (NE, NE)	2.4579 (0.5473, 11.0379) 0.2406	0.2254
HER2 IHC 2+/ISH Negative	157	5 (3.2)	152 (96.8)	NE (NE, NE)	72	1 (1.4)	71 (98.6)	NE (NE, NE)	1.6409 (0.1857, 14.5025) 0.6560	0.6529

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting									0.4359
1	220	11 (5.0)	209 (95.0) NE (NE, NE)	94	1 (1.1)	93 (98.9) NE (NE, NE)	3.8893 (0.4973, 30.4199) 0.1956	0.1633	
>=2	150	7 (4.7)	143 (95.3) NE (NE, NE)	78	2 (2.6)	76 (97.4) NE (NE, NE)	1.3317 (0.2696, 6.5792) 0.7252	0.7250	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.5429
Yes	233	13 (5.6)	220 (94.4)	NE (NE, NE)	112	2 (1.8)	110 (98.2)	NE (NE, NE)	2.4045 (0.5331, 10.8449) 0.2536	0.2392	
No	98	3 (3.1)	95 (96.9)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	1.1508 (0.1188, 11.1490) 0.9035	0.9034	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9681
<65	289	13 (4.5)	276 (95.5)	NE (NE, NE)	126	2 (1.6)	124 (98.4)	NE (NE, NE)	2.2247 (0.4947, 10.0050) 0.2972	0.2849	
>=65	82	5 (6.1)	77 (93.9)	NE (NE, NE)	46	1 (2.2)	45 (97.8)	NE (NE, NE)	2.1131 (0.2391, 18.6768) 0.5010	0.4914	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0704
<75	357	18 (5.0)	339 (95.0)	NE (NE, NE)	163	2 (1.2)	161 (98.8)	NE (NE, NE)	3.1586 (0.7245, 13.7711) 0.1258	0.1064	
>=75	14	0	14 (100)	NE (NE, NE)	9	1 (11.1)	8 (88.9)	NE (0.6, NE)	0.0000 (0.0000, ) 0.9984	0.2294	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.7697
White	175	10 (5.7)	165 (94.3)	NE (NE, NE)	85	2 (2.4)	83 (97.6)	NE (NE, NE)	1.8397 (0.3945, 8.5796) 0.4378	0.4310	
Non-White	196	8 (4.1)	188 (95.9)	NE (NE, NE)	86	1 (1.2)	85 (98.8)	NE (NE, NE)	2.8418 (0.3510, 23.0058) 0.3277	0.3062	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Region										0.3962
Asia	147	6 (4.1)	141 (95.9)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (NE, NE)	1.8671 (0.2197, 15.8694) 0.5674	0.5613
North America	58	5 (8.6)	53 (91.4)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9961	0.2378
Europe + Israel	166	7 (4.2)	159 (95.8)	NE (NE, NE)	81	2 (2.5)	79 (97.5)	NE (NE, NE)	1.5392 (0.3170, 7.4734) 0.5927	0.5900

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	199	6 (3.0)	193 (97.0)	NE (NE, NE)	95	0	95 (100)	NE (NE, NE)	0.9955	0.2053	0.1424
1	172	12 (7.0)	160 (93.0)	NE (NE, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	1.5940 (0.4447, 5.7141)	0.4707	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.5441
0	60	2 (3.3)	58 (96.7)	NE (NE, NE)	31	0	31 (100)	NE (NE, NE)	NE (NE, NE) 0.9972	0.4073	
1	107	3 (2.8)	104 (97.2)	NE (NE, NE)	48	0	48 (100)	NE (NE, NE)	NE (NE, NE) 0.9968	0.3661	
2	114	10 (8.8)	104 (91.2)	NE (NE, NE)	50	2 (4.0)	48 (96.0)	NE (NE, NE)	1.7197 (0.3706, 7.9807) 0.4888	0.4835	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 3 (3.3)	87 (96.7)	NE (NE, NE)	43 1 (2.3)	42 (97.7)	NE (NE, NE)	1.4445 (0.1503, 13.8853) 0.7501	0.7501	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.4103
PD	173	5 (2.9)	168 (97.1)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE) 0.9956	0.1829	
PR	48	3 (6.3)	45 (93.8)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	NE (NE, NE) 0.9966	0.3196	
SD	82	8 (9.8)	74 (90.2)	NE (NE, NE)	54	2 (3.7)	52 (96.3)	NE (NE, NE)	2.1127 (0.4417, 10.1048) 0.3489	0.3382	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.4760
Yes	37	2 (5.4)	35 (94.6)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9976	0.5115	
No	334	16 (4.8)	318 (95.2)	NE (NE, NE)	159	3 (1.9)	156 (98.1)	NE (NE, NE)	2.0153 (0.5795, 7.0081) 0.2704	0.2612	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.6268
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9986	0.7237	
No	347	17 (4.9)	330 (95.1)	NE (NE, NE)	165	3 (1.8)	162 (98.2)	NE (NE, NE)	2.1568 (0.6244, 7.4497) 0.2242	0.2134	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Renal function at baseline										0.1455
Normal Function	201	10 (5.0)	191 (95.0)	NE (NE, NE)	80	0	80 (100)	NE (NE, NE)	0.9940	0.0787
Mild Impairment	123	5 (4.1)	118 (95.9)	NE (NE, NE)	65	1 (1.5)	64 (98.5)	1.9940 (0.2282, 17.4208)	0.5326	0.5247
Moderate Impairment	41	3 (7.3)	38 (92.7)	NE (16.5, NE)	23	2 (8.7)	21 (91.3)	0.7464 (0.1237, 4.5035)	0.7498	0.7490

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Hepatic function at baseline											
Normal Function	170	9 (5.3)	161 (94.7)	NE (NE, NE)	88	2 (2.3)	86 (97.7)	NE (NE, NE)	2.0460 (0.4364, 9.5914) 0.3638	0.3541	0.7057
Mild Impairment	194	9 (4.6)	185 (95.4)	NE (NE, NE)	82	1 (1.2)	81 (98.8)	NE (NE, NE)	2.5619 (0.3187, 20.5941) 0.3764	0.3592	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.5363
Yes	331	17 (5.1)	314 (94.9)	NE (NE, NE)	146	3 (2.1)	143 (97.9)	NE (NE, NE)	1.9673 (0.5701, 6.7888) 0.2843	0.2755	
No	40	1 (2.5)	39 (97.5)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9976	0.4201	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.4071
Positive	329	16 (4.9)	313 (95.1)	NE (NE, NE)	152	3 (2.0)	149 (98.0)	NE (NE, NE)	1.9619 (0.5650, 6.8131) 0.2887	0.2800	
Negative	42	2 (4.8)	40 (95.2)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) 0.9974	0.4487	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.4364
Positive	331	16 (4.8)	315 (95.2)	NE (NE, NE)	155	3 (1.9)	152 (98.1)	NE (NE, NE)	1.9910 (0.5732, 6.9151)	0.2693	
Negative	40	2 (5.0)	38 (95.0)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	0.2784 (NE, NE)	0.4690	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0789
HER2 IHC 1+	214	9 (4.2)	205 (95.8)	NE (NE, NE)	100	3 (3.0)	97 (97.0)	NE (NE, NE)	0.8644 (0.2265, 3.2992) 0.8312	0.8311	
HER2 IHC 2+/ISH Negative	157	7 (4.5)	150 (95.5)	NE (NE, NE)	72	0	72 (100)	NE (NE, NE)	NE (NE, NE) 0.9947	0.1172	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.2968
1	220	6 (2.7)	214 (97.3)	NE (NE, NE)	94	2 (2.1)	92 (97.9)	NE (NE, NE)	0.9738 (0.1905, 4.9775) 0.9746	0.9747	
>=2	150	10 (6.7)	140 (93.3)	NE (NE, NE)	78	1 (1.3)	77 (98.7)	NE (NE, NE)	2.9661 (0.3703, 23.7586) 0.3058	0.2833	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.1096
Yes	233	10 (4.3)	223 (95.7)	NE (NE, NE)	112	3 (2.7)	109 (97.3)	NE (NE, NE)	1.0057 (0.2669, 3.7899) 0.9933	0.9933	
No	98	6 (6.1)	92 (93.9)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9951	0.1549	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9949
<65	289	12 (4.2)	277 (95.8)	NE (NE, NE)	126	2 (1.6)	124 (98.4)	NE (NE, NE)	1.5083 (0.3281, 6.9343) 0.5975	0.5945	
>=65	82	4 (4.9)	78 (95.1)	NE (NE, NE)	46	1 (2.2)	45 (97.8)	NE (NE, NE)	2.0515 (0.2279, 18.4698) 0.5216	0.5127	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4155
<75	357	15 (4.2)	342 (95.8)	NE (NE, NE)	163	3 (1.8)	160 (98.2)	NE (NE, NE)	1.5328 (0.4343, 5.4101) 0.5068	0.5032	
>=75	14	1 (7.1)	13 (92.9)	NE (5.9, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9985	0.4561	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.4811
White	175	7 (4.0)	168 (96.0)	NE (NE, NE)	85	2 (2.4)	83 (97.6)	NE (NE, NE)	1.1404 (0.2302, 5.6490) 0.8722	0.8721	
Non-White	196	9 (4.6)	187 (95.4)	NE (NE, NE)	86	1 (1.2)	85 (98.8)	NE (NE, NE)	2.7299 (0.3391, 21.9780) 0.3453	0.3259	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.7096
Asia	147	5 (3.4)	142 (96.6)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (NE, NE)	1.4367 (0.1618, 12.7597) 0.7450	0.7435	
North America	58	2 (3.4)	56 (96.6)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9979	0.5818	
Europe + Israel	166	9 (5.4)	157 (94.6)	NE (NE, NE)	81	2 (2.5)	79 (97.5)	NE (NE, NE)	1.6470 (0.3487, 7.7778) 0.5287	0.5246	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.8793
0	199	6 (3.0)	193 (97.0)	NE (NE, NE)	95	1 (1.1)	94 (98.9)	NE (NE, NE)	1.8064 (0.2112, 15.4516) 0.5892	0.5841	
1	172	10 (5.8)	162 (94.2)	NE (NE, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	1.5880 (0.3380, 7.4606) 0.5580	0.5546	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.6494
0	60	2 (3.3)	58 (96.7)	NE (NE, NE)	31	1 (3.2)	30 (96.8)	NE (NE, NE)	0.3684 (0.0276, 4.9181) 0.4501	0.4371	
1	107	3 (2.8)	104 (97.2)	NE (NE, NE)	48	0	48 (100)	NE (NE, NE)	NE (NE, NE) 0.9962	0.2458	
2	114	6 (5.3)	108 (94.7)	NE (NE, NE)	50	1 (2.0)	49 (98.0)	NE (NE, NE)	1.7176 (0.2004, 14.7190) 0.6216	0.6175	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	5 (5.6)	85 (94.4)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	1.3925 (0.1541, 12.5816) 0.7681	0.7671	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.0089
PD	173	4 (2.3)	169 (97.7)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE) 0.9964	0.3144	
PR	48	2 (4.2)	46 (95.8)	NE (NE, NE)	21	3 (14.3)	18 (85.7)	NE (NE, NE)	0.1845 (0.0289, 1.1795) 0.0742	0.0480	
SD	82	5 (6.1)	77 (93.9)	NE (NE, NE)	54	0	54 (100)	NE (NE, NE)	NE (NE, NE) 0.9946	0.0685	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.6114
Yes	37	1 (2.7)	36 (97.3)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.5637	
No	334	15 (4.5)	319 (95.5)	NE (NE, NE)	159	3 (1.9)	156 (98.1)	NE (NE, NE)	1.5693 (0.4453, 5.5304) 0.4832	0.4797	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.6068
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.5812	
No	347	15 (4.3)	332 (95.7)	NE (NE, NE)	165	3 (1.8)	162 (98.2)	NE (NE, NE)	1.5452 (0.4382, 5.4487) 0.4985	0.4947	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.5508
Normal Function	201	9 (4.5)	192 (95.5)	NE (NE, NE)	80	2 (2.5)	78 (97.5)	NE (NE, NE)	1.1529 (0.2409, 5.5169) 0.8586	0.8585	
Mild Impairment	123	5 (4.1)	118 (95.9)	NE (NE, NE)	65	1 (1.5)	64 (98.5)	NE (NE, NE)	1.8837 (0.2113, 16.7945) 0.5705	0.5644	
Moderate Impairment	41	2 (4.9)	39 (95.1)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9970	0.3598	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1255
Normal Function	170	5 (2.9)	165 (97.1)	NE (NE, NE)	88	0	88 (100)	NE (NE, NE)	NE (NE, NE) 0.9954	0.1715	
Mild Impairment	194	11 (5.7)	183 (94.3)	NE (NE, NE)	82	3 (3.7)	79 (96.3)	NE (NE, NE)	0.9721 (0.2632, 3.5895) 0.9661	0.9663	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.5303
Yes	331	15 (4.5)	316 (95.5)	NE (NE, NE)	146	3 (2.1)	143 (97.9)	NE (NE, NE)	1.5831 (0.4517, 5.5477) 0.4728	0.4690	
No	40	1 (2.5)	39 (97.5)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9987	0.8383	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.9999
Positive	329	16 (4.9)	313 (95.1)	NE (NE, NE)	152	3 (2.0)	149 (98.0)	NE (NE, NE)	1.6781 (0.4809, 5.8557)	0.4120	
Negative	42	0	42 (100)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.9999
Positive	331	16 (4.8)	315 (95.2)	NE (NE, NE)	155	3 (1.9)	152 (98.1)	NE (NE, NE)	1.7003 (0.4871, 5.9356)	0.4001	
Negative	40	0	40 (100)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0745
HER2 IHC 1+	214	3 (1.4)	211 (98.6)	NE (NE, NE)	100	9 (9.0)	91 (91.0)	NE (NE, NE)	0.0869 (0.0216, 0.3494) 0.0006	<0.0001	
HER2 IHC 2+/ISH Negative	157	4 (2.5)	153 (97.5)	NE (NE, NE)	72	2 (2.8)	70 (97.2)	NE (NE, NE)	0.5391 (0.0951, 3.0547) 0.4850	0.4787	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.0013
1	220	0	220 (100)	NE (NE, NE)	94	7 (7.4)	87 (92.6)	NE (NE, NE)	0.0000 (0.0000, ) 0.9943	<0.0001	
>=2	150	7 (4.7)	143 (95.3)	NE (NE, NE)	78	4 (5.1)	74 (94.9)	NE (NE, NE)	0.3828 (0.1060, 1.3828) 0.1428	0.1310	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.3626
Yes	233	1 (0.4)	232 (99.6)	NE (NE, NE)	112	4 (3.6)	108 (96.4)	NE (NE, NE)	0.0998 (0.0110, 0.9067) 0.0407	0.0122	
No	98	5 (5.1)	93 (94.9)	NE (NE, NE)	43	6 (14.0)	37 (86.0)	NE (NE, NE)	0.2156 (0.0636, 0.7309) 0.0138	0.0080	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5461
<65	289	4 (1.4)	285 (98.6)	NE (NE, NE)	126	7 (5.6)	119 (94.4)	NE (NE, NE)	0.1464 (0.0402, 0.5338) 0.0036	0.0011	
>=65	82	3 (3.7)	79 (96.3)	NE (NE, NE)	46	4 (8.7)	42 (91.3)	NE (NE, NE)	0.2673 (0.0570, 1.2528) 0.0941	0.0750	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4272
<75	357	6 (1.7)	351 (98.3)	NE (NE, NE)	163	10 (6.1)	153 (93.9)	NE (NE, NE)	0.1503 (0.0515, 0.4390) 0.0005	0.0001	
>=75	14	1 (7.1)	13 (92.9)	NE (5.1, NE)	9	1 (11.1)	8 (88.9)	NE (0.0, NE)	0.5071 (0.0311, 8.2671) 0.6335	0.6272	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.1405
White	175	1 (0.6)	174 (99.4)	NE (NE, NE)	85	0	85 (100)	NE (NE, NE)	NE (NE, NE) 0.9982	0.6291	
Non-White	196	6 (3.1)	190 (96.9)	NE (NE, NE)	86	11 (12.8)	75 (87.2)	NE (NE, NE)	0.1371 (0.0484, 0.3879) 0.0002	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.6697
Asia	147	4 (2.7)	143 (97.3)	NE (NE, NE)	63	8 (12.7)	55 (87.3)	NE (NE, NE)	0.1315 (0.0376, 0.4600) 0.0015	0.0003	
North America	58	1 (1.7)	57 (98.3)	NE (NE, NE)	28	1 (3.6)	27 (96.4)	NE (NE, NE)	0.3023 (0.0185, 4.9348) 0.4012	0.3742	
Europe + Israel	166	2 (1.2)	164 (98.8)	NE (NE, NE)	81	2 (2.5)	79 (97.5)	NE (NE, NE)	0.2170 (0.0285, 1.6510) 0.1400	0.1100	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.0118
0	199	1 (0.5)	198 (99.5)	NE (NE, NE)	95	8 (8.4)	87 (91.6)	NE (NE, NE)	0.0458 (0.0056, 0.3714) 0.0039	<0.0001	
1	172	6 (3.5)	166 (96.5)	NE (NE, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	0.3921 (0.0889, 1.7297) 0.2163	0.2035	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.0150
0	60	3 (5.0)	57 (95.0)	NE (NE, NE)	31	3 (9.7)	28 (90.3)	NE (NE, NE)	0.2637 (0.0478, 1.4534) 0.1259	0.1082	
1	107	1 (0.9)	106 (99.1)	NE (NE, NE)	48	5 (10.4)	43 (89.6)	NE (NE, NE)	0.0730 (0.0084, 0.6361) 0.0178	0.0023	
2	114	0	114 (100)	NE (NE, NE)	50	3 (6.0)	47 (94.0)	NE (NE, NE)	0.0000 (0.0000, ) 0.9967	0.0021	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	3 (3.3)	87 (96.7)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9960	0.5040	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.2910
PD	173	4 (2.3)	169 (97.7)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	0.8345 (0.0875, 7.9541)	0.8749	
PR	48	2 (4.2)	46 (95.8)	NE (16.5, NE)	21	3 (14.3)	18 (85.7)	NE (5.5, NE)	0.0506 (0.0043, 0.5894)	0.0030	
SD	82	1 (1.2)	81 (98.8)	NE (NE, NE)	54	2 (3.7)	52 (96.3)	NE (NE, NE)	0.2673 (0.0238, 3.0070)	0.2541	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 18:42; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_SAESOCPT10PAT\_2\_SAS.rtf

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DE.T.4.10.2 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.1846
Yes	37	1 (2.7)	36 (97.3)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9985	0.7055	
No	334	6 (1.8)	328 (98.2)	NE (NE, NE)	159	11 (6.9)	148 (93.1)	NE (NE, NE)	0.1491 (0.0523, 0.4245) 0.0004	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 18:42; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_SAESOCPT10PAT\_2\_SAS.rtf

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DE.T.4.10.2 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.1781
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9982	0.6374	
No	347	6 (1.7)	341 (98.3)	NE (NE, NE)	165	11 (6.7)	154 (93.3)	NE (NE, NE)	0.1469 (0.0515, 0.4188) 0.0003	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 18:42; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_SAESOCPT10PAT\_2\_SAS.rtf

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.3465
Normal Function	201	2 (1.0)	199 (99.0)	NE (NE, NE)	80	3 (3.8)	77 (96.3)	NE (NE, NE)	0.1543 (0.0228, 1.0457) 0.0556	0.0316	
Mild Impairment	123	3 (2.4)	120 (97.6)	NE (NE, NE)	65	7 (10.8)	58 (89.2)	NE (NE, NE)	0.1389 (0.0344, 0.5617) 0.0056	0.0016	
Moderate Impairment	41	2 (4.9)	39 (95.1)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	0.8564 (0.0768, 9.5473) 0.8997	0.8996	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 18:42; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_SAESOCPT10PAT\_2\_SAS.rtf

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DE.T.4.10.2 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1859
Normal Function	170	5 (2.9)	165 (97.1)	NE (NE, NE)	88	5 (5.7)	83 (94.3)	NE (NE, NE)	0.3005 (0.0833, 1.0838) 0.0662	0.0541	
Mild Impairment	194	2 (1.0)	192 (99.0)	NE (NE, NE)	82	6 (7.3)	76 (92.7)	NE (NE, NE)	0.0796 (0.0144, 0.4381) 0.0036	0.0004	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.8594
Yes	331	6 (1.8)	325 (98.2)	NE (NE, NE)	146	9 (6.2)	137 (93.8)	NE (NE, NE)	0.1851 (0.0638, 0.5373) 0.0019	0.0006	
No	40	1 (2.5)	39 (97.5)	NE (NE, NE)	26	2 (7.7)	24 (92.3)	NE (NE, NE)	0.1199 (0.0071, 2.0122) 0.1405	0.1079	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.7587
Positive	329	6 (1.8)	323 (98.2)	NE (NE, NE)	152	10 (6.6)	142 (93.4)	NE (NE, NE)	0.1618 (0.0562, 0.4658)	0.0002	
Negative	42	1 (2.4)	41 (97.6)	NE (NE, NE)	20	1 (5.0)	19 (95.0)	NE (NE, NE)	0.2865 (0.0164, 5.0118)	0.3658	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.10.2 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Injury, poisoning and procedural complications; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.8468
Positive	331	6 (1.8)	325 (98.2)	NE (NE, NE)	155	10 (6.5)	145 (93.5)	NE (NE, NE)	0.1635 (0.0567, 0.4712)	0.0002	
Negative	40	1 (2.5)	39 (97.5)	NE (NE, NE)	17	1 (5.9)	16 (94.1)	NE (NE, NE)	0.2062 (0.0107, 3.9591)	0.2583	

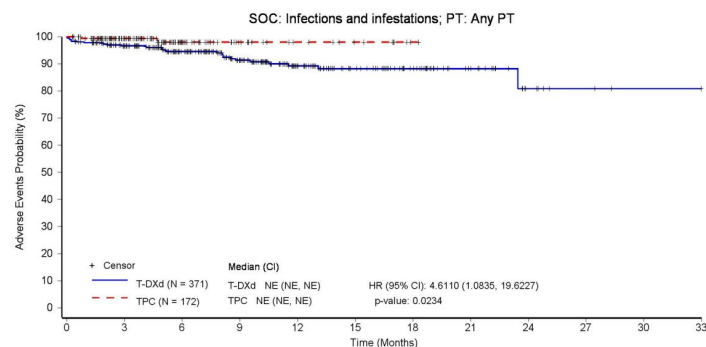
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 DE.F.4.10.3 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

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Patients still at risk:

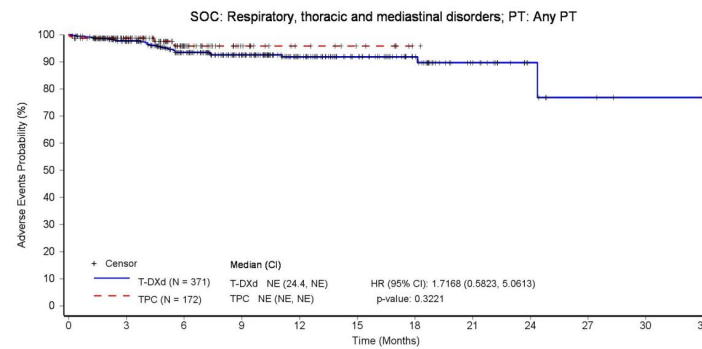
Time (Months)	T-DXd (N = 371)	TPC (N = 172)
0	371	172
3	309	107
6	230	43
9	163	20
12	100	11
15	66	7
18	42	1
21	20	0
24	7	0
27	3	0
30	1	0
33	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 DE.F.4.10.3 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

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Patients still at risk:

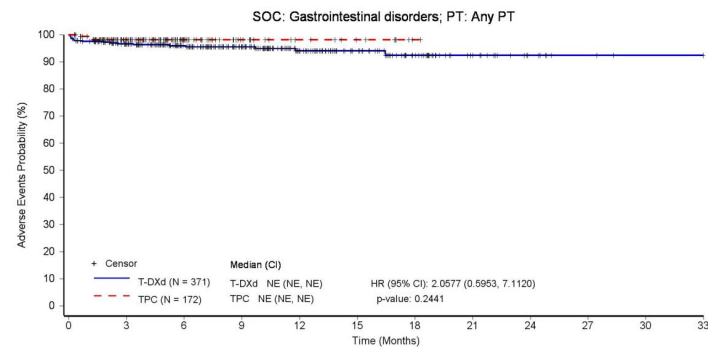
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	311	231	171	108	72	43	19	7	3	1	0
TPC (N = 172)	172	106	44	20	11	7	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 DE.F.4.10.3 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

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Patients still at risk:

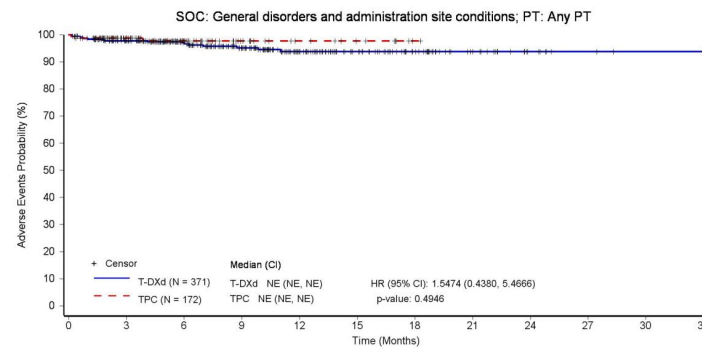
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	306	232	169	105	69	41	18	8	3	1	0
TPC (N = 172)	172	107	44	20	11	7	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

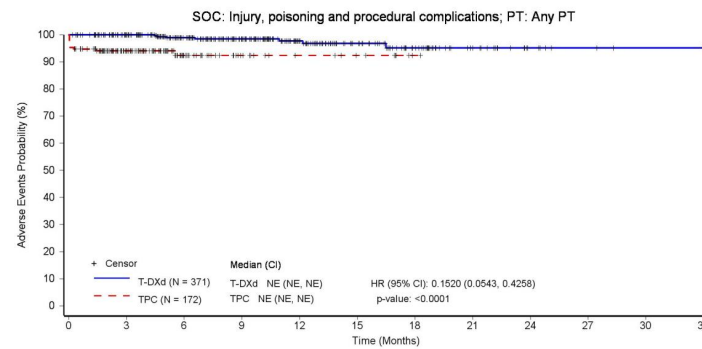
Time (Months)	T-DXd (N = 371)	TPC (N = 172)
0	371	172
3	310	107
6	233	44
9	170	20
12	107	11
15	70	7
18	42	1
21	20	0
24	8	0
27	3	0
30	1	0
33	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:54; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_SAESOCPT10PAT\_3\_SAS.rf

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 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.4.10.3 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

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 Final



Patients still at risk:

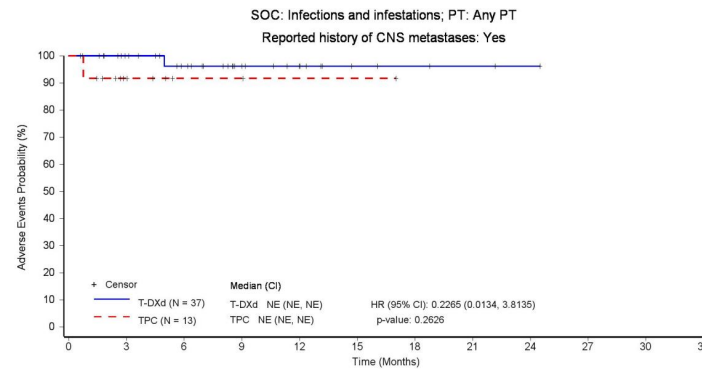
T-DXd (N = 371)	371	314	236	174	110	72	43	19	7	3	1	0
TPC (N = 172)	172	172	100	38	17	10	7	1	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:54; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_SAESOCPT10PAT\_3\_SAS.rf

Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.4.10.4 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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Patients still at risk:

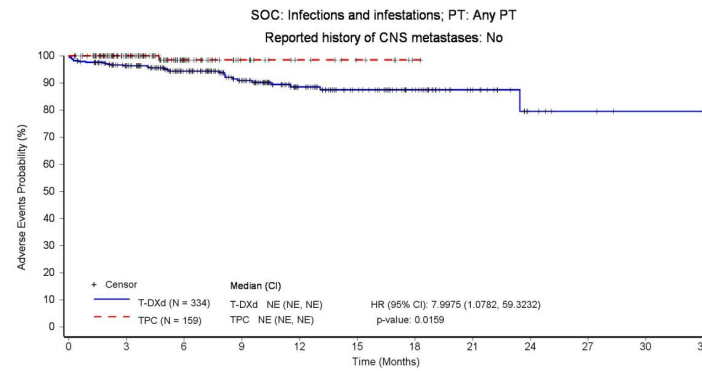
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 37)	37	30	23	14	9	4	3	2	1	0	0	0
TPC (N = 13)	13	6	2	2	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:55; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_SAESOCPT10PAT\_4\_SAS.rf

Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.4.10.4 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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 Final



Patients still at risk:

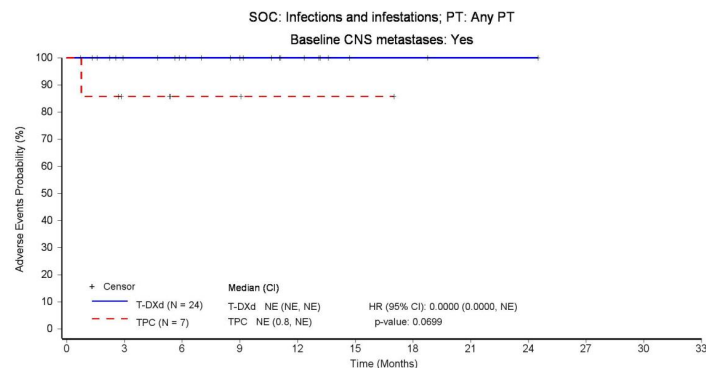
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 334)	334	279	207	149	91	62	39	18	6	3	1	0
TPC (N = 159)	159	101	41	18	10	6	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:55; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_SAESOCPT10PAT\_4\_SAS.rf

Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.4.10.4 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 24)	24	18	15	12	7	2	2	1	1	0	0	0
TPC (N = 7)	7	4	2	2	1	1	0	0	0	0	0	0

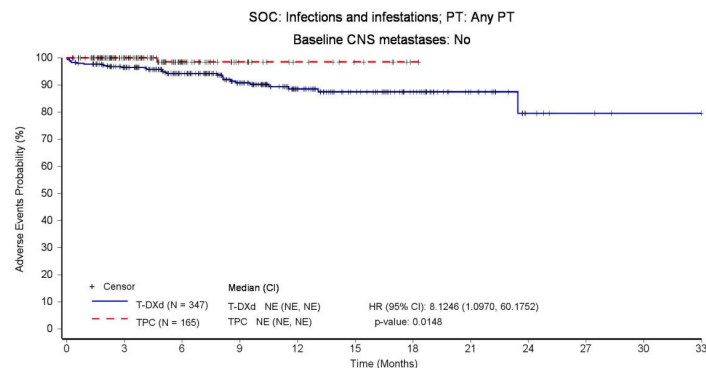
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.4.10.4 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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 Final



Patients still at risk:

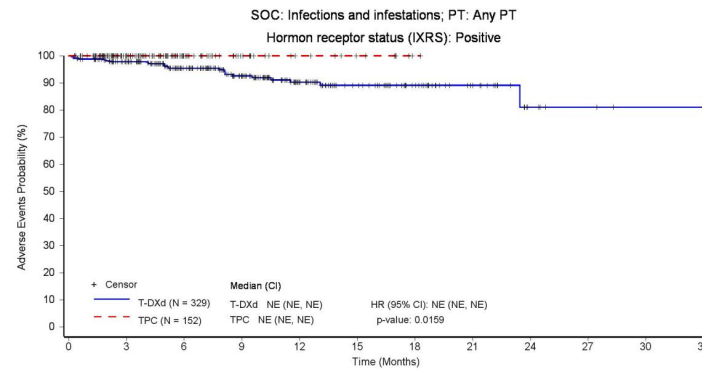
Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 347)	347	291	215	151	93	64	40	19	6	3	1	0
TPC (N = 165)	165	103	41	18	10	6	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:55; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_SAESOCPT10PAT\_4\_SAS.rf

Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.4.10.4 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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 Final



Patients still at risk:

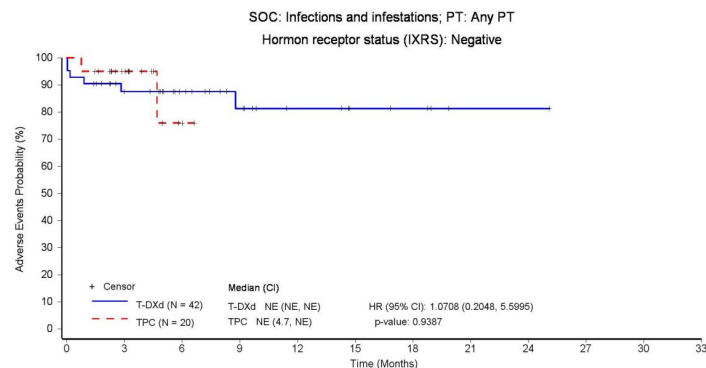
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 329)	329	280	210	150	92	61	38	19	6	3	1	0
TPC (N = 152)	152	96	41	20	11	7	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:55; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_SAESOCPT10PAT\_4\_SAS.rf

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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.4.10.4 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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 Final



Patients still at risk:

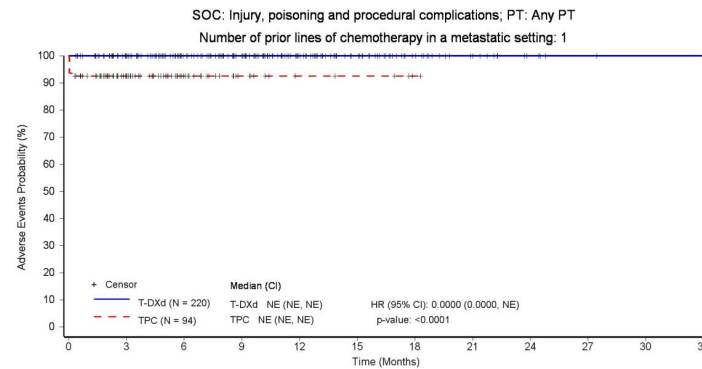
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 42)	42	29	20	13	8	5	4	1	1	0	0	0
TPC (N = 20)	20	12	2	0	0	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:55; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_SAESOCPT10PAT\_4\_SAS.rf

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 Data Intelligence – Evidence Generation  
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 DE.F.4.10.4 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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 Final



Patients still at risk:

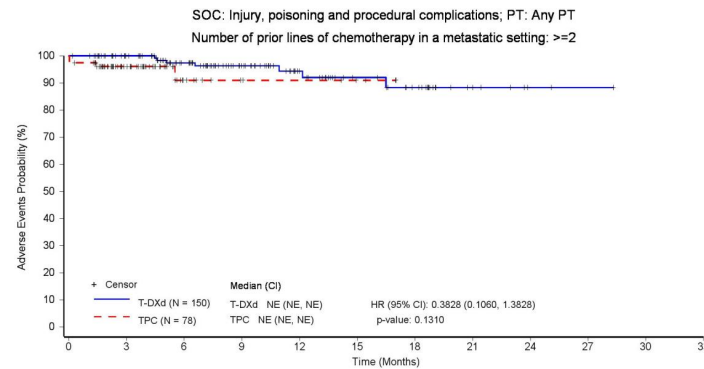
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 220)	220	186	139	108	69	45	23	12	5	2	1	0
TPC (N = 94)	94	56	25	11	5	4	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:55; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_SAESOCPT10PAT\_4\_SAS.rf

Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.4.10.4 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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 Final



Patients still at risk:

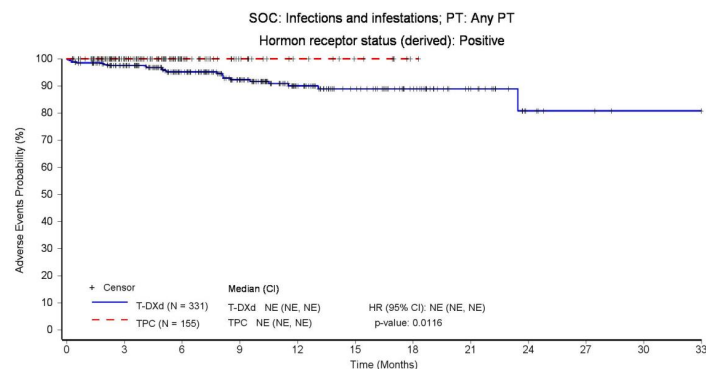
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 150)	150	127	96	65	40	26	19	6	2	1	0	0
TPC (N = 78)	78	44	13	6	5	3	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:55; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_SAESOCPT10PAT\_4\_SAS.rf

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 Data Intelligence – Evidence Generation  
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 DE.F.4.10.4 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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 Final



Patients still at risk:

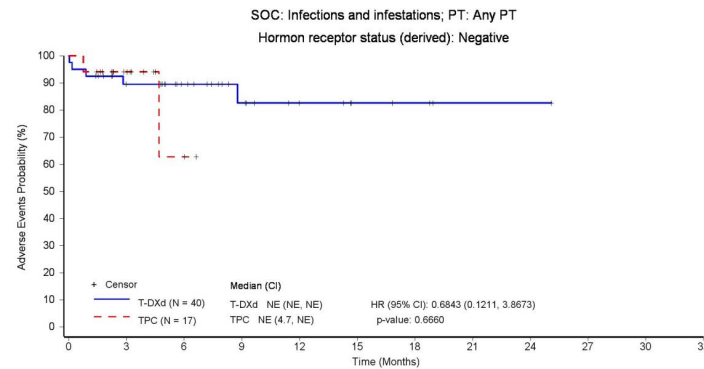
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 331)	331	280	210	151	93	62	39	19	6	3	1	0
TPC (N = 155)	155	98	41	20	11	7	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:55; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_SAESOCPT10PAT\_4\_SAS.rf

Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)  
 DE.F.4.10.4 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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Patients still at risk:

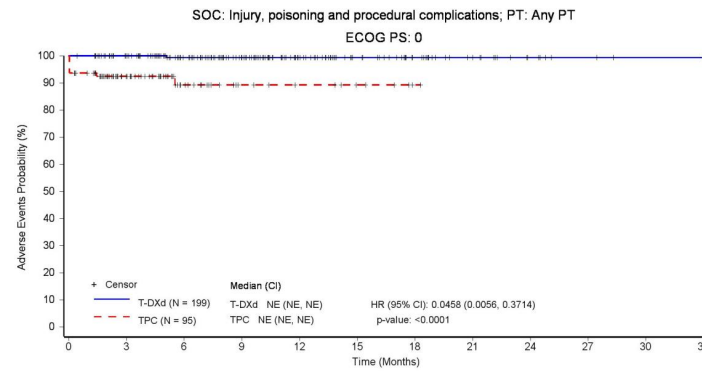
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 40)	40	29	20	12	7	4	3	1	1	0	0	0
TPC (N = 17)	17	9	2	0	0	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:55; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_SAESOCPT10PAT\_4\_SAS.rf

Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 199)	199	178	138	106	67	45	28	15	7	3	1	0
TPC (N = 95)	95	54	24	11	8	5	1	0	0	0	0	0

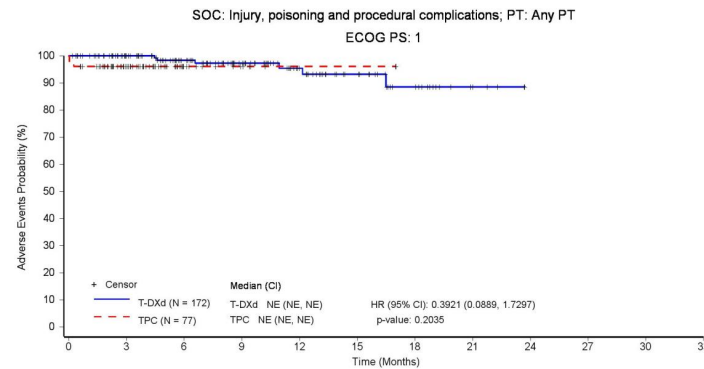
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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 Final



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 172)	172	136	98	68	43	27	15	4	0	0	0	0
TPC (N = 77)	77	46	14	6	2	2	0	0	0	0	0	0

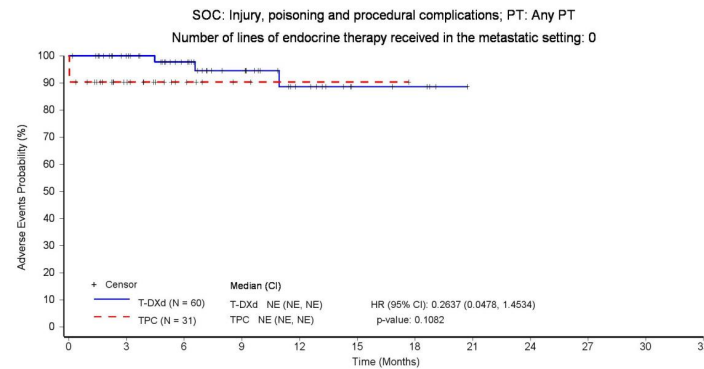
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
 Statistical analyses for AMNOG (HTA Germany)

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 Final

DE.F.4.10.4 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

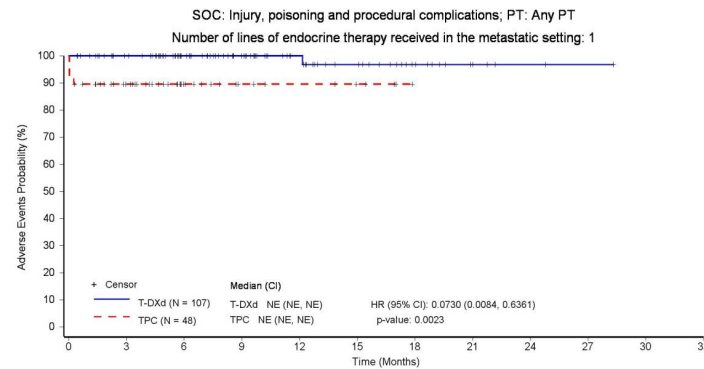
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 60)	60	49	34	23	12	5	4	0	0	0	0	0
TPC (N = 31)	31	16	6	2	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:55; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_SAESOCPT10PAT\_4\_SAS.rf

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 Data Intelligence – Evidence Generation  
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 Final



Patients still at risk:

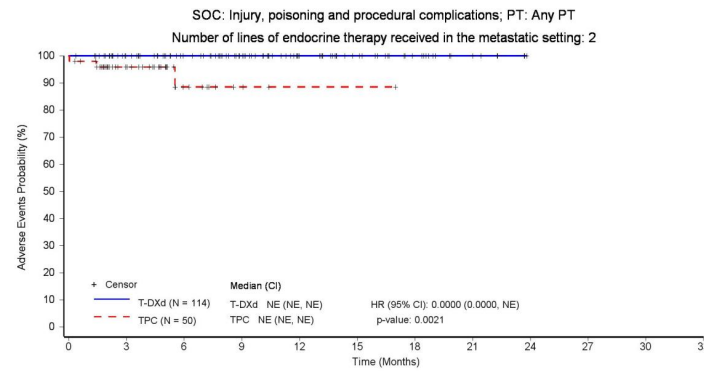
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 107)	107	91	67	47	31	21	11	4	2	1	0	0
TPC (N = 48)	48	32	15	8	6	4	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Daiichi Sankyo  
 Data Intelligence – Evidence Generation  
 DS8201-A-U303 – Destiny Breast 04 (DCO 11-Jan-2022)  
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Patients still at risk:

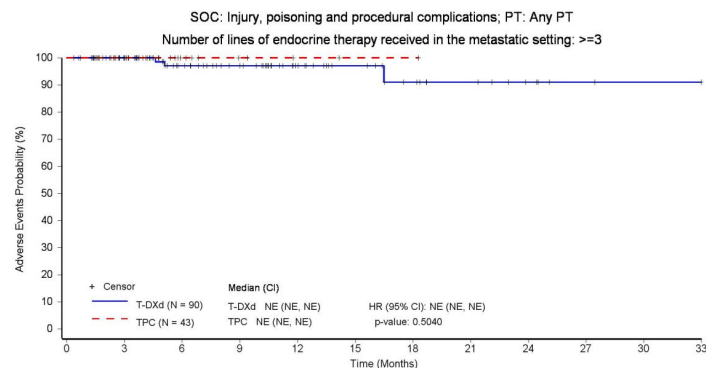
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 114)	114	93	77	60	39	26	15	6	0	0	0	0
TPC (N = 50)	50	29	9	3	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 Final



Patients still at risk:

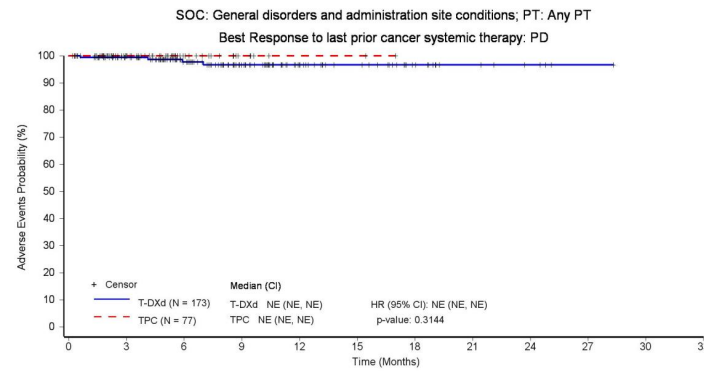
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 90)	90	81	58	44	28	20	13	9	5	2	1	0
TPC (N = 43)	43	23	8	4	2	1	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:55; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_SAESOCPT10PAT\_4\_SAS.rf

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 DE.F.4.10.4 - Serious Treatment-emergent adverse events by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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Patients still at risk:

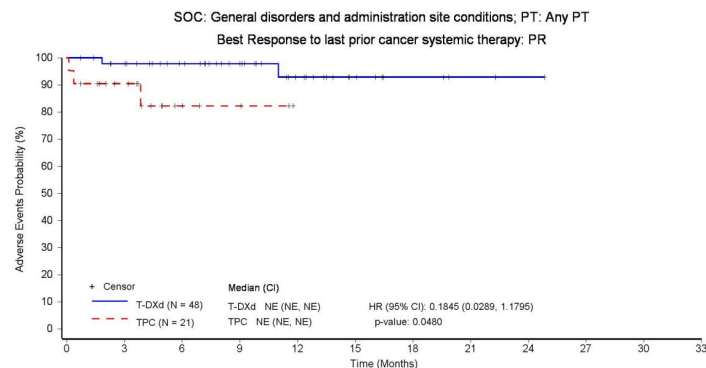
Time (Months)	T-DXd (N = 173)	TPC (N = 77)
0	173	77
3	144	45
6	102	18
9	71	6
12	40	2
15	28	2
18	15	0
21	7	0
24	4	0
27	1	0
30	0	0
33	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:55; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_SAESOCPT10PAT\_4\_SAS.rf

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Patients still at risk:

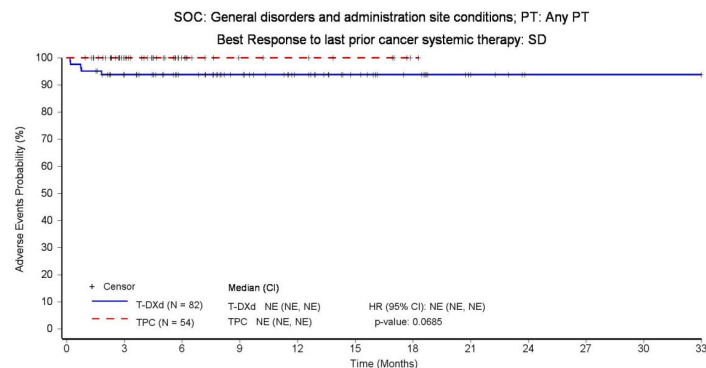
	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 48)	48	43	35	26	16	8	4	2	1	0	0	0
TPC (N = 21)	21	14	5	3	0	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 82)	82	64	50	39	29	19	13	5	1	1	1	0
TPC (N = 54)	54	35	16	8	7	5	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.11.1 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Investigations; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	89 (24.0)	70 (40.7)	
Number of subjects censored, n (%)	282 (76.0)	102 (59.3)	
Median time to first event (months) [a]	24.8	9.9	
95% Confidence Interval	[23.5, NE]	[6.0, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.3743
95% Confidence Interval			[0.2694, 0.5200]
p-value			<0.0001
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 13SEP2022 – 18:47; Program name: T4\_AESOCPT10PAT\_1\_SAS.sas; Output name: T4\_AESEVSOCPT5PER\_1\_SAS.rtf

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DE.T.4.11.1 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Investigations; PT: Neutrophil count decreased

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	31 (8.4)	49 (28.5)	
Number of subjects censored, n (%)	340 (91.6)	123 (71.5)	
Median time to first event (months) [a] 95% Confidence Interval	NE [24.8, NE]	NE [9.9, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.2115 [0.1333, 0.3354] <0.0001
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.11.1 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Investigations; PT: White blood cell count decreased

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	25 (6.7)	30 (17.4)	
Number of subjects censored, n (%)	346 (93.3)	142 (82.6)	
Median time to first event (months) [a]	NE	NE	
95% Confidence Interval	[24.8, NE]	[NE, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.2623
95% Confidence Interval			[0.1497, 0.4595]
p-value			<0.0001
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 13SEP2022 – 18:47; Program name: T4\_AESOCPT10PAT\_1\_SAS.sas; Output name: T4\_AESEVSOCPT5PER\_1\_SAS.rtf

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DE.T.4.11.1 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Investigations; PT: Platelet count decreased

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	20 (5.4)	1 (0.6)	
Number of subjects censored, n (%)	351 (94.6)	171 (99.4)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			7.4877 [0.9985, 56.1516] 0.0502
Stratified log-rank p-value [c]			0.0213

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 18:47; Program name: T4\_AESOCPT10PAT\_1\_SAS.sas; Output name: T4\_AESEVSOCPT5PER\_1\_SAS.rtf

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DE.T.4.11.1 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Investigations; PT: Alanine aminotransferase increased

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	4 (1.1)	9 (5.2)	
Number of subjects censored, n (%)	367 (98.9)	163 (94.8)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.1722 [0.0520, 0.5704] 0.0040
Stratified log-rank p-value [c]			0.0012

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.11.1 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Blood and lymphatic system disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	63 (17.0)	37 (21.5)	
Number of subjects censored, n (%)	308 (83.0)	135 (78.5)	
Median time to first event (months) [a] 95% Confidence Interval	NE [24.8, NE]	NE [15.4, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.5546 [0.3648, 0.8431] 0.0058
Stratified log-rank p-value [c]			0.0052

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 18:47; Program name: T4\_AESOCPT10PAT\_1\_SAS.sas; Output name: T4\_AESEVSOCPT5PER\_1\_SAS.rtf

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DE.T.4.11.1 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Blood and lymphatic system disorders; PT: Anaemia

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	38 (10.2)	9 (5.2)	
Number of subjects censored, n (%)	333 (89.8)	163 (94.8)	
Median time to first event (months) [a] 95% Confidence Interval	NE [24.8, NE]	NE [15.4, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.4839 [0.7099, 3.1020] 0.2941
Stratified log-rank p-value [c]			0.2907

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.11.1 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Blood and lymphatic system disorders; PT: Neutropenia

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	21 (5.7)	24 (14.0)	
Number of subjects censored, n (%)	350 (94.3)	148 (86.0)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.3266 [0.1791, 0.5957] 0.0003
Stratified log-rank p-value [c]			0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.11.1 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: General disorders and administration site conditions; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	41 (11.1)	9 (5.2)	
Number of subjects censored, n (%)	330 (88.9)	163 (94.8)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.5546 [0.7452, 3.2433] 0.2396
Stratified log-rank p-value [c]			0.2364

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

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DE.T.4.11.1 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: General disorders and administration site conditions; PT: Fatigue

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	20 (5.4)	3 (1.7)	
Number of subjects censored, n (%)	351 (94.6)	169 (98.3)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			2.5042 [0.7359, 8.5219] 0.1418
Stratified log-rank p-value [c]			0.1286

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.11.1 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Gastrointestinal disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	39 (10.5)	7 (4.1)	
Number of subjects censored, n (%)	332 (89.5)	165 (95.9)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			2.1549 [0.9561, 4.8566] 0.0641
Stratified log-rank p-value [c]			0.0583

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.11.1 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Infections and infestations; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	32 (8.6)	6 (3.5)	
Number of subjects censored, n (%)	339 (91.4)	166 (96.5)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.6675 [0.6850, 4.0592] 0.2599
Stratified log-rank p-value [c]			0.2551

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.11.1 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Metabolism and nutrition disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	31 (8.4)	8 (4.7)	
Number of subjects censored, n (%)	340 (91.6)	164 (95.3)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.4306 [0.6508, 3.1447] 0.3729
Stratified log-rank p-value [c]			0.3711

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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 Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	20 (5.4)	8 (4.7)	
Number of subjects censored, n (%)	351 (94.6)	164 (95.3)	
Median time to first event (months) [a] 95% Confidence Interval	NE [24.4, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.6203 [0.2617, 1.4705] 0.2782
Stratified log-rank p-value [c]			0.2704

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.11.1 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Nervous system disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	7 (1.9)	11 (6.4)	
Number of subjects censored, n (%)	364 (98.1)	161 (93.6)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.1848 [0.0670, 0.5097] 0.0011
Stratified log-rank p-value [c]			0.0003

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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 Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set

SOC: Skin and subcutaneous tissue disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	3 (0.8)	9 (5.2)	
Number of subjects censored, n (%)	368 (99.2)	163 (94.8)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.1347 [0.0361, 0.5022] 0.0028
Stratified log-rank p-value [c]			0.0005

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.5117
HER2 IHC 1+	214	50 (23.4)	164 (76.6)	NE (23.5, NE)	100	41 (41.0)	59 (59.0)	NE (2.4, NE)	0.3281 (0.2129, 0.5055) <0.0001	<0.0001	
HER2 IHC 2+/ISH Negative	157	39 (24.8)	118 (75.2)	24.8 (24.8, NE)	72	29 (40.3)	43 (59.7)	7.1 (6.0, NE)	0.4244 (0.2585, 0.6968) 0.0007	0.0005	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects Nsub	No. of subjects with events (%)	Median (95% CI) (months) [a]	No. of subjects Nsub	No. of subjects with events (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting									0.4185
1	220	45 (20.5)	175 (79.5) NE (23.5, NE)	94	30 (31.9)	64 (68.1) NE (6.9, NE)	0.4360 (0.2715, 0.7001) 0.0006	0.0004	
>=2	150	44 (29.3)	106 (70.7) 24.8 (19.4, NE)	78	40 (51.3)	38 (48.7) 4.2 (0.7, 13.6)	0.3155 (0.2002, 0.4973) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.4042
Yes	233	48 (20.6)	185 (79.4)	NE (NE, NE)	112	38 (33.9)	74 (66.1)	9.9 (6.0, NE)	0.4283 (0.2769, 0.6626) 0.0001	0.0001	
No	98	28 (28.6)	70 (71.4)	23.5 (23.5, NE)	43	24 (55.8)	19 (44.2)	6.9 (0.5, NE)	0.2772 (0.1575, 0.4879) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7800
<65	289	70 (24.2)	219 (75.8)	24.8 (23.5, NE)	126	49 (38.9)	77 (61.1)	9.9 (6.0, NE)	0.3740 (0.2557, 0.5471) <0.0001	<0.0001	
>=65	82	19 (23.2)	63 (76.8)	NE (NE, NE)	46	21 (45.7)	25 (54.3)	7.1 (0.7, NE)	0.3614 (0.1916, 0.6817) 0.0017	0.0011	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7208
<75	357	86 (24.1)	271 (75.9)	24.8 (23.5, NE)	163	65 (39.9)	98 (60.1)	9.9 (6.0, NE)	0.3726 (0.2664, 0.5211) <0.0001	<0.0001	
>=75	14	3 (21.4)	11 (78.6)	NE (3.5, NE)	9	5 (55.6)	4 (44.4)	7.1 (0.2, NE)	0.2776 (0.0655, 1.1757) 0.0818	0.0627	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.3047
White	175	32 (18.3)	143 (81.7)	NE (23.5, NE)	85	24 (28.2)	61 (71.8)	13.6 (6.9, NE)	0.4199 (0.2418, 0.7291) 0.0021	0.0016	
Non-White	196	57 (29.1)	139 (70.9)	24.8 (19.4, NE)	86	46 (53.5)	40 (46.5)	3.5 (0.5, NE)	0.3128 (0.2091, 0.4680) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.1048
Asia	147	48 (32.7)	99 (67.3)	24.8 (12.9, NE)	63	41 (65.1)	22 (34.9)	0.5 (0.3, 4.2)	0.2611 (0.1693, 0.4029) <0.0001	<0.0001	
North America	58	14 (24.1)	44 (75.9)	NE (NE, NE)	28	12 (42.9)	16 (57.1)	6.0 (1.0, NE)	0.3406 (0.1526, 0.7601) 0.0085	0.0064	
Europe + Israel	166	27 (16.3)	139 (83.7)	NE (23.5, NE)	81	17 (21.0)	64 (79.0)	13.6 (7.2, NE)	0.5243 (0.2795, 0.9835) 0.0443	0.0418	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											
0	199	47 (23.6)	152 (76.4)	NE (NE, NE)	95	35 (36.8)	60 (63.2)	13.6 (7.1, NE)	0.4201 (0.2684, 0.6575) 0.0001	0.0001	0.4863
1	172	42 (24.4)	130 (75.6)	23.5 (19.4, 24.8)	77	35 (45.5)	42 (54.5)	6.0 (0.9, NE)	0.3128 (0.1941, 0.5040) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1432
0	60	13 (21.7)	47 (78.3)	NE (12.5, NE)	31	16 (51.6)	15 (48.4)	2.4 (0.3, NE)	0.2369 (0.1091, 0.5144) 0.0003	<0.0001	
1	107	27 (25.2)	80 (74.8)	NE (NE, NE)	48	20 (41.7)	28 (58.3)	13.6 (3.3, NE)	0.4267 (0.2377, 0.7657) 0.0043	0.0034	
2	114	30 (26.3)	84 (73.7)	23.5 (19.4, NE)	50	14 (28.0)	36 (72.0)	NE (NE, NE)	0.6644 (0.3462, 1.2750) 0.2189	0.2300	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 (21.1)	71 (78.9)	NE (24.8, NE)	43 (46.5)	23 (53.5)	7.1 (0.5, 9.9)	0.2405 (0.1216, 0.4755) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.1298
PD	173	42 (24.3)	131 (75.7)	NE (23.5, NE)	77	28 (36.4)	49 (63.6)	NE (6.9, NE)	0.4456 (0.2718, 0.7305) 0.0014	0.0011	
PR	48	12 (25.0)	36 (75.0)	24.8 (19.4, 24.8)	21	13 (61.9)	8 (38.1)	0.5 (0.3, NE)	0.1778 (0.0758, 0.4168) 0.0001	<0.0001	
SD	82	19 (23.2)	63 (76.8)	NE (NE, NE)	54	20 (37.0)	34 (63.0)	9.9 (3.3, NE)	0.4829 (0.2550, 0.9143) 0.0254	0.0216	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.8735
Yes	37	10 (27.0)	27 (73.0)	NE (NE, NE)	13	6 (46.2)	7 (53.8)	NE (0.3, NE)	0.4595 (0.1651, 1.2790)	0.1363	
No	334	79 (23.7)	255 (76.3)	24.8 (23.5, NE)	159	64 (40.3)	95 (59.7)	9.9 (6.9, NE)	0.1365 (0.2530, 0.5027)	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.2347
Yes	24	8 (33.3)	16 (66.7)	NE (0.5, NE)	7	2 (28.6)	5 (71.4)	NE (0.3, NE)	1.2727 (0.2694, 6.0115) 0.7608	0.7638	
No	347	81 (23.3)	266 (76.7)	24.8 (23.5, NE)	165	68 (41.2)	97 (58.8)	7.2 (6.0, NE)	0.3402 (0.2432, 0.4760) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.9003
Normal Function	201	46 (22.9)	155 (77.1)	NE (NE, NE)	80	31 (38.8)	49 (61.3)	6.9 (6.0, NE)	0.3520 (0.2189, 0.5659) <0.0001	<0.0001	
Mild Impairment	123	32 (26.0)	91 (74.0)	24.8 (23.5, NE)	65	25 (38.5)	40 (61.5)	NE (1.2, NE)	0.4815 (0.2811, 0.8247) 0.0078	0.0079	
Moderate Impairment	41	11 (26.8)	30 (73.2)	19.4 (10.6, NE)	23	12 (52.2)	11 (47.8)	7.2 (0.9, NE)	0.3084 (0.1315, 0.7229) 0.0068	0.0045	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.0119
Normal Function	170	31 (18.2)	139 (81.8)	24.8 (23.5, NE)	88	39 (44.3)	49 (55.7)	9.9 (3.3, NE)	0.2350 (0.1426, 0.3871) <0.0001	<0.0001	
Mild Impairment	194	57 (29.4)	137 (70.6)	NE (12.9, NE)	82	30 (36.6)	52 (63.4)	7.2 (6.0, NE)	0.5174 (0.3277, 0.8170) 0.0047	0.0046	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.5002
Yes	331	79 (23.9)	252 (76.1)	24.8 (23.5, NE)	146	58 (39.7)	88 (60.3)	9.9 (6.9, NE)	0.3848 (0.2711, 0.5461) <0.0001	<0.0001	
No	40	10 (25.0)	30 (75.0)	NE (12.5, NE)	26	12 (46.2)	14 (53.8)	4.2 (0.5, NE)	0.2644 (0.1044, 0.6694) 0.0050	0.0029	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											
Positive	329	76 (23.1)	253 (76.9)	24.8 (23.5, NE)	152	62 (40.8)	90 (59.2)	9.9 (6.0, NE)	0.3464 (0.2446, 0.4906) <0.0001	<0.0001	0.3416
Negative	42	13 (31.0)	29 (69.0)	19.4 (7.6, NE)	20	8 (40.0)	12 (60.0)	3.3 (0.7, NE)	0.5186 (0.2044, 1.3156) 0.1668	0.1480	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (derived)											0.7697
Positive	331	77 (23.3)	254 (76.7)	24.8 (23.5, NE)	155	62 (40.0)	93 (60.0)	9.9 (6.9, NE)	0.3537 (0.2497, 0.5011) <0.0001	<0.0001	
Negative	40	12 (30.0)	28 (70.0)	NE (7.6, NE)	17	8 (47.1)	9 (52.9)	2.4 (0.5, NE)	0.4202 (0.1644, 1.0740) 0.0702	0.0591	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.9514
HER2 IHC 1+	214	17 (7.9)	197 (92.1)	NE (NE, NE)	100	27 (27.0)	73 (73.0)	NE (NE, NE)	0.2170 (0.1174, 0.4013) <0.0001	<0.0001	
HER2 IHC 2+/ISH Negative	157	14 (8.9)	143 (91.1)	NE (24.8, NE)	72	22 (30.6)	50 (69.4)	NE (6.9, NE)	0.2011 (0.1002, 0.4036) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.3733
1	220	17 (7.7)	203 (92.3)	NE (NE, NE)	94	21 (22.3)	73 (77.7)	NE (9.9, NE)	0.2550 (0.1332, 0.4883)	<0.0001	
>=2	150	14 (9.3)	136 (90.7)	NE (24.8, NE)	78	28 (35.9)	50 (64.1)	NE (4.2, NE)	0.1772 (0.0911, 0.3446)	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.0867
Yes	233	22 (9.4)	211 (90.6)	NE (NE, NE)	112	28 (25.0)	84 (75.0)	NE (9.9, NE)	0.2860 (0.1623, 0.5039) <0.0001	<0.0001	
No	98	8 (8.2)	90 (91.8)	NE (24.8, NE)	43	18 (41.9)	25 (58.1)	NE (0.5, NE)	0.1163 (0.0482, 0.2807) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6418
<65	289	24 (8.3)	265 (91.7)	NE (24.8, NE)	126	37 (29.4)	89 (70.6)	NE (9.9, NE)	0.1905 (0.1120, 0.3240) <0.0001	<0.0001	
>=65	82	7 (8.5)	75 (91.5)	NE (NE, NE)	46	12 (26.1)	34 (73.9)	NE (6.9, NE)	0.2717 (0.1065, 0.6931) 0.0064	0.0037	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1475
<75	357	31 (8.7)	326 (91.3)	NE (24.8, NE)	163	46 (28.2)	117 (71.8)	NE (9.9, NE)	0.2170 (0.1359, 0.3465)	<0.0001	
>=75	14	0	14 (100)	NE (NE, NE)	9	3 (33.3)	6 (66.7)	NE (0.2, NE)	0.0000 (0.0000, ) 0.9973	0.0215	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.8847
White	175	5 (2.9)	170 (97.1)	NE (NE, NE)	85	11 (12.9)	74 (87.1)	NE (NE, NE)	0.1685 (0.0577, 0.4922) 0.0011	0.0002	
Non-White	196	26 (13.3)	170 (86.7)	NE (24.8, NE)	86	38 (44.2)	48 (55.8)	9.9 (1.2, NE)	0.1935 (0.1159, 0.3231) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.0130
Asia	147	23 (15.6)	124 (84.4)	NE (24.8, NE)	63	36 (57.1)	27 (42.9)	0.9 (0.5, NE)	0.1554 (0.0906, 0.2666) <0.0001	<0.0001	
North America	58	1 (1.7)	57 (98.3)	NE (NE, NE)	28	9 (32.1)	19 (67.9)	NE (2.4, NE)	0.0420 (0.0053, 0.3326) 0.0027	<0.0001	
Europe + Israel	166	7 (4.2)	159 (95.8)	NE (NE, NE)	81	4 (4.9)	77 (95.1)	NE (NE, NE)	0.6163 (0.1761, 2.1575) 0.4490	0.4454	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.4094
0	199	18 (9.0)	181 (91.0)	NE (NE, NE)	95	24 (25.3)	71 (74.7)	NE (9.9, NE)	0.2583 (0.1390, 0.4797)	<0.0001	
1	172	13 (7.6)	159 (92.4)	24.8 (NE, NE)	77	25 (32.5)	52 (67.5)	NE (6.9, NE)	0.1630 (0.0809, 0.3282)	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.4682
0	60	2 (3.3)	58 (96.7)	NE (NE, NE)	31	9 (29.0)	22 (71.0)	NE (6.9, NE)	0.0846 (0.0179, 0.4003) 0.0018	<0.0001	
1	107	9 (8.4)	98 (91.6)	NE (NE, NE)	48	13 (27.1)	35 (72.9)	NE (NE, NE)	0.2508 (0.1068, 0.5893) 0.0015	0.0006	
2	114	11 (9.6)	103 (90.4)	NE (NE, NE)	50	12 (24.0)	38 (76.0)	NE (NE, NE)	0.2994 (0.1305, 0.6865) 0.0044	0.0029	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	9 (10.0)	81 (90.0)	NE (24.8, NE)	43	15 (34.9)	28 (65.1)	9.9 (9.9, NE)	0.1677 (0.0692, 0.4065) 0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.0682
PD	173	8 (4.6)	165 (95.4)	NE (NE, NE)	77	18 (23.4)	59 (76.6)	NE (NE, NE)	0.1598 (0.0690, 0.3702)	<0.0001	
PR	48	5 (10.4)	43 (89.6)	24.8 (NE, NE)	21	10 (47.6)	11 (52.4)	NE (0.3, NE)	0.1162 (0.0362, 0.3733)	<0.0001	
SD	82	13 (15.9)	69 (84.1)	NE (NE, NE)	54	16 (29.6)	38 (70.4)	NE (9.9, NE)	0.3947 (0.1877, 0.8299)	0.0112	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.8408
Yes	37	4 (10.8)	33 (89.2)	NE (NE, NE)	13	5 (38.5)	8 (61.5)	NE (0.3, NE)	0.1752 (0.0418, 0.7352)	0.0080	
No	334	27 (8.1)	307 (91.9)	NE (24.8, NE)	159	44 (27.7)	115 (72.3)	NE (9.9, NE)	0.2090 (0.1279, 0.3417)	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.5808
Yes	24	3 (12.5)	21 (87.5)	NE (NE, NE)	7	2 (28.6)	5 (71.4)	NE (0.3, NE)	0.2781 (0.0391, 1.9774) 0.2010	0.1731	
No	347	28 (8.1)	319 (91.9)	NE (24.8, NE)	165	47 (28.5)	118 (71.5)	NE (9.9, NE)	0.2018 (0.1249, 0.3260) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.1691
Normal Function	201	14 (7.0)	187 (93.0)	NE (NE, NE)	80	22 (27.5)	58 (72.5)	9.9 (6.9, NE)	0.1661 (0.0827, 0.3335) <0.0001	<0.0001	
Mild Impairment	123	16 (13.0)	107 (87.0)	24.8 (24.8, NE)	65	18 (27.7)	47 (72.3)	NE (NE, NE)	0.3424 (0.1720, 0.6816) 0.0023	0.0016	
Moderate Impairment	41	1 (2.4)	40 (97.6)	NE (NE, NE)	23	7 (30.4)	16 (69.6)	NE (2.4, NE)	0.0679 (0.0083, 0.5531) 0.0120	0.0009	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1861
Normal Function	170	14 (8.2)	156 (91.8)	NE (24.8, NE)	88	30 (34.1)	58 (65.9)	NE (6.9, NE)	0.1626 (0.0839, 0.3148) <0.0001	<0.0001	
Mild Impairment	194	17 (8.8)	177 (91.2)	NE (NE, NE)	82	18 (22.0)	64 (78.0)	NE (NE, NE)	0.2960 (0.1510, 0.5803) 0.0004	0.0002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.4421
Yes	331	28 (8.5)	303 (91.5)	NE (24.8, NE)	146	40 (27.4)	106 (72.6)	NE (9.9, NE)	0.2246 (0.1370, 0.3683) <0.0001	<0.0001	
No	40	3 (7.5)	37 (92.5)	NE (NE, NE)	26	9 (34.6)	17 (65.4)	NE (3.3, NE)	0.1184 (0.0304, 0.4612) 0.0021	0.0004	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.4363
Positive	329	30 (9.1)	299 (90.9)	NE (24.8, NE)	152	45 (29.6)	107 (70.4)	NE (9.9, NE)	0.2164 (0.1348, 0.3474) <0.0001	<0.0001	
Negative	42	1 (2.4)	41 (97.6)	NE (NE, NE)	20	4 (20.0)	16 (80.0)	NE (3.3, NE)	0.0951 (0.0105, 0.8637) 0.0366	0.0099	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.5472
Positive	331	30 (9.1)	301 (90.9)	NE (24.8, NE)	155	46 (29.7)	109 (70.3)	NE (9.9, NE)	0.2143 (0.1338, 0.3434)	<0.0001	
Negative	40	1 (2.5)	39 (97.5)	NE (NE, NE)	17	3 (17.6)	14 (82.4)	NE (2.4, NE)	0.1224 (0.0126, 1.1886)	0.0314	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 18:47; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_AESEVSOCPT5PER\_2\_SAS.rtf

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.6003
HER2 IHC 1+	214	15 (7.0)	199 (93.0)	NE (NE, NE)	100	20 (20.0)	80 (80.0)	NE (10.4, NE)	0.2338 (0.1157, 0.4724) 0.0001	<0.0001	
HER2 IHC 2+/ISH Negative	157	10 (6.4)	147 (93.6)	NE (24.8, NE)	72	10 (13.9)	62 (86.1)	NE (NE, NE)	0.3169 (0.1265, 0.7941) 0.0142	0.0099	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.5022
1	220	11 (5.0)	209 (95.0)	NE (NE, NE)	94	10 (10.6)	84 (89.4)	NE (10.4, NE)	0.3328 (0.1377, 0.8045) 0.0146	0.0106	
>=2	150	14 (9.3)	136 (90.7)	NE (24.8, NE)	78	20 (25.6)	58 (74.4)	NE (NE, NE)	0.2346 (0.1133, 0.4859) 0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											
Yes	233	13 (5.6)	220 (94.4)	NE (NE, NE)	112	13 (11.6)	99 (88.4)	NE (NE, NE)	0.3677 (0.1675, 0.8073) 0.0126	0.0097	0.4113
No	98	8 (8.2)	90 (91.8)	NE (24.8, NE)	43	11 (25.6)	32 (74.4)	NE (10.4, NE)	0.2071 (0.0792, 0.5413) 0.0013	0.0004	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0971
<65	289	16 (5.5)	273 (94.5)	NE (24.8, NE)	126	23 (18.3)	103 (81.7)	NE (NE, NE)	0.1966 (0.0996, 0.3880) <0.0001	<0.0001	
>=65	82	9 (11.0)	73 (89.0)	NE (NE, NE)	46	7 (15.2)	39 (84.8)	NE (10.4, NE)	0.5596 (0.2054, 1.5244) 0.2562	0.2506	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5090
<75	357	24 (6.7)	333 (93.3)	NE (24.8, NE)	163	29 (17.8)	134 (82.2)	NE (NE, NE)	0.2548 (0.1444, 0.4496) <0.0001	<0.0001	
>=75	14	1 (7.1)	13 (92.9)	NE (NE, NE)	9	1 (11.1)	8 (88.9)	NE (10.4, NE)	0.6944 (0.0433, 11.1240) 0.7966	0.7955	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.7048
White	175	7 (4.0)	168 (96.0)	NE (NE, NE)	85	8 (9.4)	77 (90.6)	NE (NE, NE)	0.3020 (0.1061, 0.8599) 0.0249	0.0185	
Non-White	196	18 (9.2)	178 (90.8)	NE (24.8, NE)	86	22 (25.6)	64 (74.4)	NE (10.4, NE)	0.2379 (0.1234, 0.4584) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.9264
Asia	147	17 (11.6)	130 (88.4)	NE (24.8, NE)	63	20 (31.7)	43 (68.3)	NE (7.6, NE)	0.2261 (0.1141, 0.4479) <0.0001	<0.0001	
North America	58	3 (5.2)	55 (94.8)	NE (NE, NE)	28	4 (14.3)	24 (85.7)	NE (NE, NE)	0.2736 (0.0574, 1.3047) 0.1039	0.0850	
Europe + Israel	166	5 (3.0)	161 (97.0)	NE (NE, NE)	81	6 (7.4)	75 (92.6)	NE (NE, NE)	0.3032 (0.0901, 1.0199) 0.0538	0.0422	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.5958
0	199	12 (6.0)	187 (94.0)	NE (NE, NE)	95	16 (16.8)	79 (83.2)	NE (NE, NE)	0.2399 (0.1111, 0.5181) 0.0003	<0.0001	
1	172	13 (7.6)	159 (92.4)	24.8 (19.4, 24.8)	77	14 (18.2)	63 (81.8)	NE (10.4, NE)	0.2927 (0.1307, 0.6552) 0.0028	0.0015	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.0075
0	60	2 (3.3)	58 (96.7)	NE (NE, NE)	31	9 (29.0)	22 (71.0)	NE (NE, NE)	0.0995 (0.0215, 0.4609)	0.0003	
1	107	6 (5.6)	101 (94.4)	NE (NE, NE)	48	9 (18.8)	39 (81.3)	NE (10.4, NE)	0.2194 (0.0770, 0.6247)	0.0019	
2	114	12 (10.5)	102 (89.5)	NE (19.4, NE)	50	3 (6.0)	47 (94.0)	NE (NE, NE)	1.1933 (0.3258, 4.3709)	0.7846	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	5 (5.6)	85 (94.4)	NE (24.8, NE)	43	9 (20.9)	34 (79.1)	NE (NE, NE)	0.1776 (0.0544, 0.5797) 0.0042	0.0013	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.1579
PD	173	8 (4.6)	165 (95.4)	NE (NE, NE)	77	16 (20.8)	61 (79.2)	NE (7.6, NE)	0.1634 (0.0683, 0.3907)	<0.0001	
PR	48	4 (8.3)	44 (91.7)	24.8 (19.4, 24.8)	21	5 (23.8)	16 (76.2)	NE (NE, NE)	0.1243 (0.0232, 0.6660)	0.0046	
SD	82	8 (9.8)	74 (90.2)	NE (NE, NE)	54	7 (13.0)	47 (87.0)	NE (10.4, NE)	0.6170 (0.2203, 1.7283)	0.3560	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.0502
Yes	37	7 (18.9)	30 (81.1)	NE (NE, NE)	13	2 (15.4)	11 (84.6)	NE (NE, NE)	1.1620 (0.2412, 5.5971)	0.8399	
No	334	18 (5.4)	316 (94.6)	NE (24.8, NE)	159	28 (17.6)	131 (82.4)	NE (NE, NE)	0.1870 (0.0993, 0.3522)	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0017
Yes	24	6 (25.0)	18 (75.0)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9951	0.1556	
No	347	19 (5.5)	328 (94.5)	NE (24.8, NE)	165	30 (18.2)	135 (81.8)	NE (NE, NE)	0.1859 (0.1007, 0.3431) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.3694
Normal Function	201	9 (4.5)	192 (95.5)	NE (NE, NE)	80	13 (16.3)	67 (83.8)	NE (NE, NE)	0.1876 (0.0771, 0.4562) 0.0002	<0.0001	
Mild Impairment	123	12 (9.8)	111 (90.2)	24.8 (24.8, NE)	65	10 (15.4)	55 (84.6)	NE (NE, NE)	0.4803 (0.2024, 1.1395) 0.0962	0.0934	
Moderate Impairment	41	4 (9.8)	37 (90.2)	19.4 (19.4, NE)	23	5 (21.7)	18 (78.3)	NE (7.6, NE)	0.2843 (0.0677, 1.1940) 0.0858	0.0676	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.3787
Normal Function	170	14 (8.2)	156 (91.8)	NE (24.8, NE)	88	20 (22.7)	68 (77.3)	NE (NE, NE)	0.2475 (0.1199, 0.5108) 0.0002	<0.0001	
Mild Impairment	194	11 (5.7)	183 (94.3)	NE (NE, NE)	82	9 (11.0)	73 (89.0)	NE (10.4, NE)	0.3376 (0.1352, 0.8430) 0.0200	0.0154	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1732
Yes	331	22 (6.6)	309 (93.4)	NE (24.8, NE)	146	22 (15.1)	124 (84.9)	NE (NE, NE)	0.3184 (0.1729, 0.5866) 0.0002	0.0001	
No	40	3 (7.5)	37 (92.5)	NE (19.4, NE)	26	8 (30.8)	18 (69.2)	NE (0.5, NE)	0.1125 (0.0233, 0.5428) 0.0065	0.0013	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.7568
Positive	329	20 (6.1)	309 (93.9)	NE (24.8, NE)	152	25 (16.4)	127 (83.6)	NE (NE, NE)	0.2574 (0.1398, 0.4737) <0.0001	<0.0001	
Negative	42	5 (11.9)	37 (88.1)	19.4 (19.4, NE)	20	5 (25.0)	15 (75.0)	NE (0.9, NE)	0.2727 (0.0651, 1.1417) 0.0753	0.0559	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.2657
Positive	331	22 (6.6)	309 (93.4)	NE (24.8, NE)	155	24 (15.5)	131 (84.5)	NE (NE, NE)	0.2890 (0.1575, 0.5303) 0.0001	<0.0001	
Negative	40	3 (7.5)	37 (92.5)	NE (NE, NE)	17	6 (35.3)	11 (64.7)	NE (0.5, NE)	0.1245 (0.0251, 0.6180) 0.0108	0.0025	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.2457
HER2 IHC 1+	214	10 (4.7)	204 (95.3)	NE (NE, NE)	100	0	100 (100)	NE (NE, NE)	NE (NE, NE) 0.9942	0.0934	
HER2 IHC 2+/ISH Negative	157	10 (6.4)	147 (93.6)	NE (NE, NE)	72	1 (1.4)	71 (98.6)	NE (NE, NE)	4.1663 (0.5306, 32.7147) 0.1747	0.1407	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.3119
1	220	9 (4.1)	211 (95.9)	NE (NE, NE)	94	0	94 (100)	NE (NE, NE)	NE (NE, NE) 0.9942	0.0909	
>=2	150	11 (7.3)	139 (92.7)	NE (NE, NE)	78	1 (1.3)	77 (98.7)	NE (NE, NE)	4.4261 (0.5626, 34.8217) 0.1575	0.1233	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.9997
Yes	233	9 (3.9)	224 (96.1)	NE (NE, NE)	112	0	112 (100)	NE (NE, NE)	NE (NE, NE) 0.9934	0.0423	
No	98	9 (9.2)	89 (90.8)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9943	0.1012	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5952
<65	289	18 (6.2)	271 (93.8)	NE (NE, NE)	126	1 (0.8)	125 (99.2)	NE (NE, NE)	5.6697 (0.7486, 42.9425) 0.0930	0.0583	
>=65	82	2 (2.4)	80 (97.6)	NE (NE, NE)	46	0	46 (100)	NE (NE, NE)	NE (NE, NE) 0.9967	0.2865	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9996
<75	357	20 (5.6)	337 (94.4)	NE (NE, NE)	163	1 (0.6)	162 (99.4)	NE (NE, NE)	6.9041 (0.9186, 51.8924) 0.0605	0.0294	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.4418
White	175	5 (2.9)	170 (97.1)	NE (NE, NE)	85	0	85 (100)	NE (NE, NE)	NE (NE, NE) 0.9953	0.1496	
Non-White	196	15 (7.7)	181 (92.3)	NE (NE, NE)	86	1 (1.2)	85 (98.8)	NE (NE, NE)	4.9294 (0.6447, 37.6899) 0.1243	0.0888	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.7338
Asia	147	15 (10.2)	132 (89.8)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (NE, NE)	4.7808 (0.6253, 36.5514) 0.1317	0.0964	
North America	58	1 (1.7)	57 (98.3)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9978	0.4872	
Europe + Israel	166	4 (2.4)	162 (97.6)	NE (NE, NE)	81	0	81 (100)	NE (NE, NE)	NE (NE, NE) 0.9958	0.2042	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.1241
0	199	14 (7.0)	185 (93.0)	NE (NE, NE)	95	0	95 (100)	NE (NE, NE)	NE (NE, NE) 0.9924	0.0231	
1	172	6 (3.5)	166 (96.5)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	2.1035 (0.2481, 17.8321) 0.4953	0.4858	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.2635
0	60	2 (3.3)	58 (96.7)	NE (NE, NE)	31	1 (3.2)	30 (96.8)	NE (NE, NE)	1.0338 (0.0937, 11.4012) 0.9783	0.9818	
1	107	4 (3.7)	103 (96.3)	NE (NE, NE)	48	0	48 (100)	NE (NE, NE)	NE (NE, NE) 0.9958	0.2186	
2	114	9 (7.9)	105 (92.1)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	NE (NE, NE) 0.9943	0.0935	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects with events Nsub	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events Nsub	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	5 (5.6)	85 (94.4) NE (NE, NE)	43	0	43 (100) NE (NE, NE)	NE (NE, NE) 0.9957	0.1961	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.4753
PD	173	8 (4.6)	165 (95.4)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	3.1715 (0.3937, 25.5492)	0.2537	
PR	48	2 (4.2)	46 (95.8)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	0.2782 (NE, NE)	0.4733	
SD	82	5 (6.1)	77 (93.9)	NE (NE, NE)	54	0	54 (100)	NE (NE, NE)	0.9975 (NE, NE)	0.0691	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.6261
Yes	37	3 (8.1)	34 (91.9)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9965	0.3079	
No	334	17 (5.1)	317 (94.9)	NE (NE, NE)	159	1 (0.6)	158 (99.4)	NE (NE, NE)	5.9582 (0.7846, 45.2476) 0.0845	0.0502	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Baseline CNS metastases										0.7068
Yes	24	2 (8.3)	22 (91.7)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE) 0.9972	0.4232	
No	347	18 (5.2)	329 (94.8)	NE (NE, NE)	165	1 (0.6)	164 (99.4)	6.3894 (0.8446, 48.3340) 0.0724	0.0395	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.1013
Normal Function	201	13 (6.5)	188 (93.5)	NE (NE, NE)	80	0	80 (100)	NE (NE, NE)	NE (NE, NE) 0.9934	0.0574	
Mild Impairment	123	6 (4.9)	117 (95.1)	NE (NE, NE)	65	0	65 (100)	NE (NE, NE)	NE (NE, NE) 0.9946	0.0913	
Moderate Impairment	41	1 (2.4)	40 (97.6)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	0.4781 (0.0296, 7.7115) 0.6030	0.5948	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1456
Normal Function	170	6 (3.5)	164 (96.5)	NE (NE, NE)	88	1 (1.1)	87 (98.9)	NE (NE, NE)	2.4267 (0.2885, 20.4122) 0.4145	0.3999	
Mild Impairment	194	14 (7.2)	180 (92.8)	NE (NE, NE)	82	0	82 (100)	NE (NE, NE)	NE (NE, NE) 0.9927	0.0330	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.0984
Yes	331	16 (4.8)	315 (95.2)	NE (NE, NE)	146	0	146 (100)	NE (NE, NE)	NE (NE, NE) 0.9920	0.0184	
No	40	4 (10.0)	36 (90.0)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	1.6600 (0.1730, 15.9267) 0.6605	0.6574	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.0404
Positive	329	18 (5.5)	311 (94.5)	NE (NE, NE)	152	0	152 (100)	NE (NE, NE)	NE (NE, NE) 0.9914	0.0111	
Negative	42	2 (4.8)	40 (95.2)	NE (NE, NE)	20	1 (5.0)	19 (95.0)	NE (NE, NE)	0.4755 (0.0297, 7.6035) 0.5991	0.5907	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.0344
Positive	331	18 (5.4)	313 (94.6)	NE (NE, NE)	155	0	155 (100)	NE (NE, NE)	NE (NE, NE) 0.9914	0.0105	
Negative	40	2 (5.0)	38 (95.0)	NE (NE, NE)	17	1 (5.9)	16 (94.1)	NE (NE, NE)	0.4230 (0.0264, 6.7645) 0.5430	0.5304	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0099
HER2 IHC 1+	214	0	214 (100)	NE (NE, NE)	100	6 (6.0)	94 (94.0)	NE (NE, NE)	0.0000 (0.0000, ) 0.9947	0.0001	
HER2 IHC 2+/ISH Negative	157	4 (2.5)	153 (97.5)	NE (NE, NE)	72	3 (4.2)	69 (95.8)	NE (13.6, NE)	0.4826 (0.1052, 2.2144) 0.3486	0.3381	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.0067
1	220	0	220 (100)	NE (NE, NE)	94	6 (6.4)	88 (93.6)	NE (NE, NE)	0.0000 (0.0000, ) 0.9949	<0.0001	
>=2	150	4 (2.7)	146 (97.3)	NE (NE, NE)	78	3 (3.8)	75 (96.2)	NE (13.6, NE)	0.5259 (0.1135, 2.4356) 0.4112	0.4030	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.2366
Yes	233	1 (0.4)	232 (99.6)	NE (NE, NE)	112	8 (7.1)	104 (92.9)	NE (NE, NE)	0.0539 (0.0067, 0.4322) 0.0060	0.0001	
No	98	1 (1.0)	97 (99.0)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (13.6, NE)	0.2345 (0.0145, 3.7825) 0.3067	0.2658	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2585
<65	289	4 (1.4)	285 (98.6)	NE (NE, NE)	126	7 (5.6)	119 (94.4)	NE (13.6, NE)	0.1844 (0.0523, 0.6499)	0.0034	
>=65	82	0	82 (100)	NE (NE, NE)	46	2 (4.3)	44 (95.7)	NE (NE, NE)	0.0000 (0.0000, ) 0.9966	0.0576	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9995
<75	357	4 (1.1)	353 (98.9)	NE (NE, NE)	163	9 (5.5)	154 (94.5)	NE (13.6, NE)	0.1549 (0.0463, 0.5182) 0.0025	0.0006	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.7907
White	175	2 (1.1)	173 (98.9)	NE (NE, NE)	85	4 (4.7)	81 (95.3)	NE (13.6, NE)	0.1812 (0.0314, 1.0478) 0.0564	0.0338	
Non-White	196	2 (1.0)	194 (99.0)	NE (NE, NE)	86	5 (5.8)	81 (94.2)	NE (NE, NE)	0.1453 (0.0278, 0.7578) 0.0221	0.0082	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.6892
Asia	147	1 (0.7)	146 (99.3)	NE (NE, NE)	63	4 (6.3)	59 (93.7)	NE (NE, NE)	0.0940 (0.0104, 0.8478) 0.0351	0.0088	
North America	58	1 (1.7)	57 (98.3)	NE (NE, NE)	28	1 (3.6)	27 (96.4)	NE (NE, NE)	0.4805 (0.0300, 7.6835) 0.6043	0.5964	
Europe + Israel	166	2 (1.2)	164 (98.8)	NE (NE, NE)	81	4 (4.9)	77 (95.1)	NE (13.6, NE)	0.1683 (0.0296, 0.9582) 0.0446	0.0243	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.8324
0	199	2 (1.0)	197 (99.0)	NE (NE, NE)	95	4 (4.2)	91 (95.8)	NE (13.6, NE)	0.1772 (0.0312, 1.0057) 0.0508	0.0289	
1	172	2 (1.2)	170 (98.8)	NE (NE, NE)	77	5 (6.5)	72 (93.5)	NE (NE, NE)	0.1538 (0.0295, 0.8033) 0.0264	0.0109	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.0072
0	60	1 (1.7)	59 (98.3)	NE (NE, NE)	31	0	31 (100)	NE (NE, NE)	NE (NE, NE) 0.9983	0.6464	
1	107	0	107 (100)	NE (NE, NE)	48	7 (14.6)	41 (85.4)	NE (13.6, NE)	0.0000 (0.0000, ) 0.9944	<0.0001	
2	114	2 (1.8)	112 (98.2)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	NE (NE, NE) 0.9969	0.3475	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	1 (1.1)	89 (98.9)	NE (NE, NE)	43	2 (4.7)	41 (95.3)	NE (NE, NE)	0.1839 (0.0162, 2.0847) 0.1716	0.1268	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.0335
PD	173	4 (2.3)	169 (97.7)	NE (NE, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	0.7899 (0.1428, 4.3679)	0.7862	
PR	48	0	48 (100)	NE (NE, NE)	21	2 (9.5)	19 (90.5)	NE (NE, NE)	0.7869 (0.0000, )	0.0162	
SD	82	0	82 (100)	NE (NE, NE)	54	4 (7.4)	50 (92.6)	NE (NE, NE)	0.9972 (0.0000, )	0.0113	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											NE
Yes	37	0	37 (100)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE)		
No	334	4 (1.2)	330 (98.8)	NE (NE, NE)	159	9 (5.7)	150 (94.3)	NE (NE, NE)	0.1651 (0.0495, 0.5500)	0.0009	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.9994
Yes	24	0	24 (100)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE)		
No	347	4 (1.2)	343 (98.8)	NE (NE, NE)	165	9 (5.5)	156 (94.5)	NE (NE, NE)	0.1635 (0.0490, 0.5454)	0.0009	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.4631
Normal Function	201	3 (1.5)	198 (98.5)	NE (NE, NE)	80	5 (6.3)	75 (93.8)	NE (NE, NE)	0.2184 (0.0520, 0.9174) 0.0377	0.0224	
Mild Impairment	123	0	123 (100)	NE (NE, NE)	65	2 (3.1)	63 (96.9)	NE (NE, NE)	0.0000 (0.0000, ) 0.9966	0.0499	
Moderate Impairment	41	1 (2.4)	40 (97.6)	NE (NE, NE)	23	2 (8.7)	21 (91.3)	NE (13.6, NE)	0.2419 (0.0218, 2.6808) 0.2475	0.2096	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1338
Normal Function	170	0	170 (100)	NE (NE, NE)	88	3 (3.4)	85 (96.6)	NE (13.6, NE)	0.0000 (0.0000, ) 0.9968	0.0016	
Mild Impairment	194	4 (2.1)	190 (97.9)	NE (NE, NE)	82	6 (7.3)	76 (92.7)	NE (NE, NE)	0.2428 (0.0677, 0.8706) 0.0298	0.0186	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Run date: 13SEP2022 – 18:47; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_AESEVSOCPT5PER\_2\_SAS.rtf

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.4273
Yes	331	4 (1.2)	327 (98.8)	NE (NE, NE)	146	8 (5.5)	138 (94.5)	NE (NE, NE)	0.1735 (0.0511, 0.5891) 0.0050	0.0016	
No	40	0	40 (100)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	0.0000 (0.0000, ) 0.9975	0.2148	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.0160
Positive	329	2 (0.6)	327 (99.4)	NE (NE, NE)	152	9 (5.9)	143 (94.1)	NE (NE, NE)	0.0757 (0.0160, 0.3592)	0.0012	<0.0001
Negative	42	2 (4.8)	40 (95.2)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) 0.9968		0.3203

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Alanine aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.0200
Positive	331	2 (0.6)	329 (99.4)	NE (NE, NE)	155	9 (5.8)	146 (94.2)	NE (NE, NE)	0.0766 (0.0161, 0.3641)	0.0012	<0.0001
Negative	40	2 (5.0)	38 (95.0)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) 0.9969		0.3473

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.7118
HER2 IHC 1+	214	41 (19.2)	173 (80.8)	NE (NE, NE)	100	23 (23.0)	77 (77.0)	NE (NE, NE)	0.5999 (0.3564, 1.0099) 0.0545	0.0525	
HER2 IHC 2+/ISH Negative	157	22 (14.0)	135 (86.0)	NE (24.8, NE)	72	14 (19.4)	58 (80.6)	15.4 (15.4, NE)	0.4909 (0.2454, 0.9819) 0.0443	0.0405	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.0579
1	220	30 (13.6)	190 (86.4)	NE (NE, NE)	94	23 (24.5)	71 (75.5)	15.4 (15.4, NE)	0.3976 (0.2277, 0.6941) 0.0012	0.0008	
>=2	150	33 (22.0)	117 (78.0)	24.8 (24.8, NE)	78	14 (17.9)	64 (82.1)	NE (NE, NE)	0.8772 (0.4639, 1.6586) 0.6868	0.6874	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.8486
Yes	233	34 (14.6)	199 (85.4)	NE (NE, NE)	112	22 (19.6)	90 (80.4)	NE (15.4, NE)	0.5540 (0.3201, 0.9590) 0.0349	0.0329	
No	98	22 (22.4)	76 (77.6)	24.8 (24.8, NE)	43	11 (25.6)	32 (74.4)	NE (NE, NE)	0.5489 (0.2618, 1.1510) 0.1123	0.1076	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4623
<65	289	41 (14.2)	248 (85.8)	NE (24.8, NE)	126	24 (19.0)	102 (81.0)	NE (15.4, NE)	0.5198 (0.3094, 0.8735) 0.0135	0.0122	
>=65	82	22 (26.8)	60 (73.2)	NE (12.0, NE)	46	13 (28.3)	33 (71.7)	NE (4.3, NE)	0.7128 (0.3558, 1.4283) 0.3398	0.3362	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1007
<75	357	59 (16.5)	298 (83.5)	NE (24.8, NE)	163	36 (22.1)	127 (77.9)	NE (15.4, NE)	0.5172 (0.3377, 0.7921) 0.0024	0.0021	
>=75	14	4 (28.6)	10 (71.4)	NE (3.4, NE)	9	1 (11.1)	8 (88.9)	NE (2.3, NE)	2.6461 (0.2948, 23.7549) 0.3848	0.3663	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.5839
White	175	30 (17.1)	145 (82.9)	NE (NE, NE)	85	17 (20.0)	68 (80.0)	NE (15.4, NE)	0.6536 (0.3568, 1.1975) 0.1687	0.1658	
Non-White	196	33 (16.8)	163 (83.2)	NE (24.8, NE)	86	20 (23.3)	66 (76.7)	NE (NE, NE)	0.4814 (0.2716, 0.8531) 0.0123	0.0107	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.6746
Asia	147	22 (15.0)	125 (85.0)	NE (24.8, NE)	63	10 (15.9)	53 (84.1)	NE (NE, NE)	0.6190 (0.2865, 1.3373) 0.2223	0.2176	
North America	58	9 (15.5)	49 (84.5)	NE (NE, NE)	28	4 (14.3)	24 (85.7)	NE (NE, NE)	0.8437 (0.2540, 2.8033) 0.7815	0.7862	
Europe + Israel	166	32 (19.3)	134 (80.7)	NE (NE, NE)	81	23 (28.4)	58 (71.6)	NE (15.4, NE)	0.4982 (0.2889, 0.8591) 0.0122	0.0109	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.8236
0	199	29 (14.6)	170 (85.4)	NE (NE, NE)	95	18 (18.9)	77 (81.1)	NE (15.4, NE)	0.5285 (0.2901, 0.9630) 0.0372	0.0343	
1	172	34 (19.8)	138 (80.2)	24.8 (NE, NE)	77	19 (24.7)	58 (75.3)	NE (NE, NE)	0.5749 (0.3217, 1.0274) 0.0617	0.0593	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.7062
0	60	9 (15.0)	51 (85.0)	NE (14.6, NE)	31	8 (25.8)	23 (74.2)	NE (2.9, NE)	0.3641 (0.1290, 1.0275) 0.0563	0.0471	
1	107	18 (16.8)	89 (83.2)	NE (NE, NE)	48	13 (27.1)	35 (72.9)	15.4 (15.4, NE)	0.4799 (0.2331, 0.9879) 0.0463	0.0423	
2	114	24 (21.1)	90 (78.9)	NE (NE, NE)	50	11 (22.0)	39 (78.0)	NE (NE, NE)	0.7562 (0.3668, 1.5591) 0.4491	0.4484	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	12 (13.3)	78 (86.7)	NE (24.8, NE)	43	5 (11.6)	38 (88.4)	NE (NE, NE)	0.6260 (0.2114, 1.8533) 0.3977	0.3942	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.3824
PD	173	31 (17.9)	142 (82.1)	NE (NE, NE)	77	18 (23.4)	59 (76.6)	NE (NE, NE)	0.5299 (0.2920, 0.9614)	0.0347	
PR	48	7 (14.6)	41 (85.4)	24.8 (NE, NE)	21	6 (28.6)	15 (71.4)	NE (0.7, NE)	0.2623 (0.0811, 0.8482)	0.0170	
SD	82	17 (20.7)	65 (79.3)	NE (NE, NE)	54	11 (20.4)	43 (79.6)	NE (15.4, NE)	0.8221 (0.3809, 1.7747)	0.6144	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.5324
Yes	37	1 (2.7)	36 (97.3)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	0.3466 (0.0217, 5.5478)	0.4343	
No	334	62 (18.6)	272 (81.4)	NE (24.8, NE)	159	36 (22.6)	123 (77.4)	NE (15.4, NE)	0.4539 (0.3832, 0.8878)	0.5833 (0.3832, 0.8878)	0.0112

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.1211
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	2 (28.6)	5 (71.4)	NE (0.3, NE)	0.1376 (0.0124, 1.5209) 0.1057	0.0583	
No	347	62 (17.9)	285 (82.1)	NE (24.8, NE)	165	35 (21.2)	130 (78.8)	NE (15.4, NE)	0.5964 (0.3902, 0.9116) 0.0170	0.0161	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.1242
Normal Function	201	25 (12.4)	176 (87.6)	NE (NE, NE)	80	17 (21.3)	63 (78.8)	NE (NE, NE)	0.4082 (0.2162, 0.7709) 0.0057	0.0045	
Mild Impairment	123	21 (17.1)	102 (82.9)	24.8 (24.8, NE)	65	14 (21.5)	51 (78.5)	15.4 (15.4, NE)	0.5342 (0.2645, 1.0790) 0.0805	0.0761	
Moderate Impairment	41	15 (36.6)	26 (63.4)	NE (5.1, NE)	23	6 (26.1)	17 (73.9)	NE (2.9, NE)	1.2026 (0.4655, 3.1069) 0.7032	0.7033	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.8014
Normal Function	170	28 (16.5)	142 (83.5)	NE (24.8, NE)	88	19 (21.6)	69 (78.4)	NE (NE, NE)	0.5093 (0.2793, 0.9288) 0.0278	0.0257	
Mild Impairment	194	33 (17.0)	161 (83.0)	NE (NE, NE)	82	18 (22.0)	64 (78.0)	NE (15.4, NE)	0.5757 (0.3207, 1.0333) 0.0643	0.0608	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.4955
Yes	331	55 (16.6)	276 (83.4)	NE (24.8, NE)	146	33 (22.6)	113 (77.4)	NE (15.4, NE)	0.5332 (0.3432, 0.8285) 0.0052	0.0046	
No	40	8 (20.0)	32 (80.0)	NE (14.6, NE)	26	4 (15.4)	22 (84.6)	NE (NE, NE)	0.7258 (0.2001, 2.6317) 0.6258	0.6142	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.9980
Positive	329	55 (16.7)	274 (83.3)	NE (24.8, NE)	152	32 (21.1)	120 (78.9)	NE (15.4, NE)	0.5581 (0.3573, 0.8716) 0.0104	0.0096	
Negative	42	8 (19.0)	34 (81.0)	NE (10.6, NE)	20	5 (25.0)	15 (75.0)	NE (2.9, NE)	0.5883 (0.1852, 1.8682) 0.3682	0.3674	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.7435
Positive	331	57 (17.2)	274 (82.8)	NE (24.8, NE)	155	33 (21.3)	122 (78.7)	NE (15.4, NE)	0.5724 (0.3692, 0.8873)	0.0119	
Negative	40	6 (15.0)	34 (85.0)	NE (10.6, NE)	17	4 (23.5)	13 (76.5)	NE (2.9, NE)	0.4561 (0.1207, 1.7239)	0.2397	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.5343
HER2 IHC 1+	214	25 (11.7)	189 (88.3)	NE (NE, NE)	100	5 (5.0)	95 (95.0)	NE (NE, NE)	1.8346 (0.6952, 4.8410) 0.2203	0.2141	
HER2 IHC 2+/ISH Negative	157	13 (8.3)	144 (91.7)	NE (24.8, NE)	72	4 (5.6)	68 (94.4)	NE (15.4, NE)	0.9718 (0.3072, 3.0744) 0.9612	0.9601	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.2667
1	220	19 (8.6)	201 (91.4)	NE (NE, NE)	94	6 (6.4)	88 (93.6)	NE (15.4, NE)	1.0018 (0.3940, 2.5470) 0.9970	0.9983	
>=2	150	19 (12.7)	131 (87.3)	NE (24.8, NE)	78	3 (3.8)	75 (96.2)	NE (NE, NE)	2.4670 (0.7199, 8.4536) 0.1507	0.1379	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.5341
Yes	233	16 (6.9)	217 (93.1)	NE (NE, NE)	112	5 (4.5)	107 (95.5)	NE (15.4, NE)	1.2664 (0.4570, 3.5091) 0.6497	0.6498	
No	98	17 (17.3)	81 (82.7)	NE (24.8, NE)	43	3 (7.0)	40 (93.0)	NE (NE, NE)	1.7429 (0.5047, 6.0188) 0.3796	0.3740	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7298
<65	289	26 (9.0)	263 (91.0)	NE (24.8, NE)	126	6 (4.8)	120 (95.2)	NE (15.4, NE)	1.3570 (0.5496, 3.3503) 0.5080	0.5055	
>=65	82	12 (14.6)	70 (85.4)	NE (NE, NE)	46	3 (6.5)	43 (93.5)	NE (NE, NE)	1.8267 (0.5087, 6.5590) 0.3556	0.3507	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8808
<75	357	36 (10.1)	321 (89.9)	NE (24.8, NE)	163	8 (4.9)	155 (95.1)	NE (15.4, NE)	1.4890 (0.6832, 3.2452) 0.3165	0.3134	
>=75	14	2 (14.3)	12 (85.7)	NE (4.5, NE)	9	1 (11.1)	8 (88.9)	NE (2.3, NE)	1.1575 (0.1041, 12.8742) 0.9053	0.9052	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.7244
White	175	14 (8.0)	161 (92.0)	NE (NE, NE)	85	3 (3.5)	82 (96.5)	NE (15.4, NE)	1.8271 (0.5178, 6.4474) 0.3488	0.3424	
Non-White	196	24 (12.2)	172 (87.8)	NE (24.8, NE)	86	6 (7.0)	80 (93.0)	NE (NE, NE)	1.2340 (0.4962, 3.0692) 0.6510	0.6507	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.6027
Asia	147	20 (13.6)	127 (86.4)	NE (24.8, NE)	63	4 (6.3)	59 (93.7)	NE (NE, NE)	1.4619 (0.4909, 4.3537) 0.4952	0.4936	
North America	58	8 (13.8)	50 (86.2)	NE (NE, NE)	28	1 (3.6)	27 (96.4)	NE (NE, NE)	3.3037 (0.4092, 26.6705) 0.2621	0.2346	
Europe + Israel	166	10 (6.0)	156 (94.0)	NE (NE, NE)	81	4 (4.9)	77 (95.1)	NE (15.4, NE)	0.9045 (0.2766, 2.9581) 0.8681	0.8667	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.2709
0	199	18 (9.0)	181 (91.0)	NE (NE, NE)	95	6 (6.3)	89 (93.7)	NE (15.4, NE)	1.0350 (0.4055, 2.6419) 0.9426	0.9410	
1	172	20 (11.6)	152 (88.4)	24.8 (NE, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	2.2415 (0.6533, 7.6905) 0.1994	0.1883	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.9791
0	60	6 (10.0)	54 (90.0)	NE (14.6, NE)	31	2 (6.5)	29 (93.5)	NE (NE, NE)	0.9822 (0.1871, 5.1578)	0.9832	
1	107	11 (10.3)	96 (89.7)	NE (NE, NE)	48	3 (6.3)	45 (93.8)	NE (15.4, NE)	1.4110 (0.3907, 5.0959)	0.5973	
2	114	14 (12.3)	100 (87.7)	NE (NE, NE)	50	3 (6.0)	47 (94.0)	NE (NE, NE)	1.7199 (0.4895, 6.0434)	0.3930	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	7 (7.8)	83 (92.2)	NE (24.8, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	1.5865 (0.1837, 13.7002) 0.6748	0.6722	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.6265
PD	173	18 (10.4)	155 (89.6)	NE (NE, NE)	77	4 (5.2)	73 (94.8)	NE (NE, NE)	1.4995 (0.4992, 4.5041)	0.4686	
PR	48	4 (8.3)	44 (91.7)	24.8 (NE, NE)	21	2 (9.5)	19 (90.5)	NE (NE, NE)	0.3791 (0.0582, 2.4683)	0.2994	
SD	82	9 (11.0)	73 (89.0)	NE (NE, NE)	54	3 (5.6)	51 (94.4)	NE (15.4, NE)	1.5754 (0.4206, 5.9007)	0.4970	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.5664
Yes	37	1 (2.7)	36 (97.3)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.5533	
No	334	37 (11.1)	297 (88.9)	NE (24.8, NE)	159	9 (5.7)	150 (94.3)	NE (15.4, NE)	1.4360 (0.6847, 3.0115) 0.3382	0.3359	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.2246
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	1 (14.3)	6 (85.7)	NE (0.7, NE)	0.2979 (0.0186, 4.7641) 0.3919	0.3631	
No	347	37 (10.7)	310 (89.3)	NE (24.8, NE)	165	8 (4.8)	157 (95.2)	NE (15.4, NE)	1.5934 (0.7330, 3.4636) 0.2396	0.2362	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.9644
Normal Function	201	15 (7.5)	186 (92.5)	NE (NE, NE)	80	3 (3.8)	77 (96.3)	NE (NE, NE)	1.4045 (0.3988, 4.9462) 0.5970	0.5950	
Mild Impairment	123	11 (8.9)	112 (91.1)	24.8 (24.8, NE)	65	3 (4.6)	62 (95.4)	15.4 (15.4, NE)	1.3363 (0.3570, 5.0018) 0.6668	0.6666	
Moderate Impairment	41	10 (24.4)	31 (75.6)	NE (12.0, NE)	23	3 (13.0)	20 (87.0)	NE (NE, NE)	1.7381 (0.4773, 6.3298) 0.4018	0.3972	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1971
Normal Function	170	15 (8.8)	155 (91.2)	NE (24.8, NE)	88	2 (2.3)	86 (97.7)	NE (NE, NE)	2.6949 (0.6049, 12.0053) 0.1934	0.1764	
Mild Impairment	194	21 (10.8)	173 (89.2)	NE (NE, NE)	82	7 (8.5)	75 (91.5)	NE (15.4, NE)	0.9422 (0.3941, 2.2524) 0.8935	0.8939	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.6092
Yes	331	32 (9.7)	299 (90.3)	NE (24.8, NE)	146	8 (5.5)	138 (94.5)	NE (15.4, NE)	1.3406 (0.6107, 2.9426) 0.4649	0.4637	
No	40	6 (15.0)	34 (85.0)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	2.2229 (0.2505, 19.7227) 0.4732	0.4638	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.6887
Positive	329	32 (9.7)	297 (90.3)	NE (24.8, NE)	152	8 (5.3)	144 (94.7)	NE (15.4, NE)	1.3618 (0.6198, 2.9921)	0.4402	
Negative	42	6 (14.3)	36 (85.7)	NE (10.6, NE)	20	1 (5.0)	19 (95.0)	NE (NE, NE)	1.9813 (0.2285, 17.1831)	0.5272	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.8659
Positive	331	34 (10.3)	297 (89.7)	NE (24.8, NE)	155	8 (5.2)	147 (94.8)	NE (15.4, NE)	1.4846 (0.6795, 3.2436)	0.3183	
Negative	40	4 (10.0)	36 (90.0)	NE (10.6, NE)	17	1 (5.9)	16 (94.1)	NE (2.9, NE)	1.0049 (0.1019, 9.9149)	0.9966	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.7866
HER2 IHC 1+	214	13 (6.1)	201 (93.9)	NE (NE, NE)	100	14 (14.0)	86 (86.0)	NE (NE, NE)	0.3298 (0.1520, 0.7156) 0.0050	0.0033	
HER2 IHC 2+/ISH Negative	157	8 (5.1)	149 (94.9)	NE (NE, NE)	72	10 (13.9)	62 (86.1)	NE (NE, NE)	0.3149 (0.1231, 0.8053) 0.0159	0.0111	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.6604
1	220	11 (5.0)	209 (95.0)	NE (NE, NE)	94	13 (13.8)	81 (86.2)	NE (NE, NE)	0.2873 (0.1265, 0.6525) 0.0029	0.0016	
>=2	150	10 (6.7)	140 (93.3)	NE (NE, NE)	78	11 (14.1)	67 (85.9)	NE (NE, NE)	0.3868 (0.1627, 0.9196) 0.0316	0.0260	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.5262
Yes	233	14 (6.0)	219 (94.0)	NE (NE, NE)	112	14 (12.5)	98 (87.5)	NE (NE, NE)	0.3747 (0.1752, 0.8017) 0.0114	0.0088	
No	98	5 (5.1)	93 (94.9)	NE (NE, NE)	43	7 (16.3)	36 (83.7)	NE (NE, NE)	0.2476 (0.0776, 0.7899) 0.0183	0.0110	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) with incidence  $\geq 5\%$  in at least one arm -  
Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4478
<65	289	13 (4.5)	276 (95.5)	NE (NE, NE)	126	16 (12.7)	110 (87.3)	NE (NE, NE)	0.2708 (0.1273, 0.5762) 0.0007	0.0003	
$\geq 65$	82	8 (9.8)	74 (90.2)	NE (NE, NE)	46	8 (17.4)	38 (82.6)	NE (NE, NE)	0.4829 (0.1808, 1.2900) 0.1465	0.1417	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0299
<75	357	19 (5.3)	338 (94.7)	NE (NE, NE)	163	24 (14.7)	139 (85.3)	NE (NE, NE)	0.2839 (0.1534, 0.5257) 0.0001	<0.0001	
>=75	14	2 (14.3)	12 (85.7)	NE (3.4, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9978	0.2335	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.5028
White	175	13 (7.4)	162 (92.6)	NE (NE, NE)	85	13 (15.3)	72 (84.7)	NE (NE, NE)	0.3968 (0.1820, 0.8651) 0.0201	0.0162	
Non-White	196	8 (4.1)	188 (95.9)	NE (NE, NE)	86	11 (12.8)	75 (87.2)	NE (NE, NE)	0.2468 (0.0969, 0.6286) 0.0034	0.0016	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.2365
Asia	147	2 (1.4)	145 (98.6)	NE (NE, NE)	63	3 (4.8)	60 (95.2)	NE (NE, NE)	0.2795 (0.0467, 1.6731) 0.1627	0.1362	
North America	58	0	58 (100)	NE (NE, NE)	28	2 (7.1)	26 (92.9)	NE (NE, NE)	0.0000 (0.0000, ) 0.9968	0.0371	
Europe + Israel	166	19 (11.4)	147 (88.6)	NE (NE, NE)	81	19 (23.5)	62 (76.5)	NE (NE, NE)	0.3761 (0.1971, 0.7176) 0.0030	0.0022	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.6220
0	199	9 (4.5)	190 (95.5)	NE (NE, NE)	95	9 (9.5)	86 (90.5)	NE (NE, NE)	0.3576 (0.1389, 0.9204) 0.0330	0.0265	
1	172	12 (7.0)	160 (93.0)	NE (NE, NE)	77	15 (19.5)	62 (80.5)	NE (NE, NE)	0.2940 (0.1357, 0.6373) 0.0019	0.0010	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.5177
0	60	3 (5.0)	57 (95.0)	NE (NE, NE)	31	6 (19.4)	25 (80.6)	NE (NE, NE)	0.2394 (0.0599, 0.9579) 0.0433	0.0282	
1	107	5 (4.7)	102 (95.3)	NE (NE, NE)	48	9 (18.8)	39 (81.3)	NE (NE, NE)	0.2058 (0.0686, 0.6177) 0.0048	0.0019	
2	114	10 (8.8)	104 (91.2)	NE (NE, NE)	50	7 (14.0)	43 (86.0)	NE (NE, NE)	0.5122 (0.1908, 1.3745) 0.1840	0.1766	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	3 (3.3)	87 (96.7)	NE (NE, NE)	43	2 (4.7)	41 (95.3)	NE (NE, NE)	0.4441 (0.0693, 2.8452) 0.3917	0.3802	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.3849
PD	173	13 (7.5)	160 (92.5)	NE (NE, NE)	77	14 (18.2)	63 (81.8)	NE (NE, NE)	0.2952 (0.1356, 0.6429)	0.0012	
PR	48	1 (2.1)	47 (97.9)	NE (NE, NE)	21	3 (14.3)	18 (85.7)	NE (NE, NE)	0.1277 (0.0132, 1.2332)	0.0353	
SD	82	6 (7.3)	76 (92.7)	NE (NE, NE)	54	6 (11.1)	48 (88.9)	NE (NE, NE)	0.6186 (0.1991, 1.9216)	0.4030	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.2020
Yes	37	0	37 (100)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	0.0000 (0.0000, ) 0.9980	0.0916	
No	334	21 (6.3)	313 (93.7)	NE (NE, NE)	159	23 (14.5)	136 (85.5)	NE (NE, NE)	0.3494 (0.1915, 0.6378) 0.0006	0.0004	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.1762
Yes	24	0	24 (100)	NE (NE, NE)	7	1 (14.3)	6 (85.7)	NE (0.3, NE)	0.0000 (0.0000, ) 0.9983	0.0641	
No	347	21 (6.1)	326 (93.9)	NE (NE, NE)	165	23 (13.9)	142 (86.1)	NE (NE, NE)	0.3477 (0.1904, 0.6349) 0.0006	0.0003	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.1832
Normal Function	201	8 (4.0)	193 (96.0)	NE (NE, NE)	80	13 (16.3)	67 (83.8)	NE (NE, NE)	0.1914 (0.0772, 0.4746) 0.0004	<0.0001	
Mild Impairment	123	8 (6.5)	115 (93.5)	NE (NE, NE)	65	8 (12.3)	57 (87.7)	NE (NE, NE)	0.4000 (0.1455, 1.0994) 0.0757	0.0671	
Moderate Impairment	41	5 (12.2)	36 (87.8)	NE (NE, NE)	23	3 (13.0)	20 (87.0)	NE (NE, NE)	0.8244 (0.1964, 3.4604) 0.7920	0.7975	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.2713
Normal Function	170	10 (5.9)	160 (94.1)	NE (NE, NE)	88	16 (18.2)	72 (81.8)	NE (NE, NE)	0.2399 (0.1068, 0.5388) 0.0005	0.0002	
Mild Impairment	194	11 (5.7)	183 (94.3)	NE (NE, NE)	82	8 (9.8)	74 (90.2)	NE (NE, NE)	0.5062 (0.2016, 1.2710) 0.1472	0.1403	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.5229
Yes	331	20 (6.0)	311 (94.0)	NE (NE, NE)	146	21 (14.4)	125 (85.6)	NE (NE, NE)	0.3358 (0.1802, 0.6258) 0.0006	0.0003	
No	40	1 (2.5)	39 (97.5)	NE (NE, NE)	26	3 (11.5)	23 (88.5)	NE (NE, NE)	0.2083 (0.0217, 2.0028) 0.1743	0.1321	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.8237
Positive	329	19 (5.8)	310 (94.2)	NE (NE, NE)	152	21 (13.8)	131 (86.2)	NE (NE, NE)	0.3295 (0.1752, 0.6196)	0.0003	
Negative	42	2 (4.8)	40 (95.2)	NE (NE, NE)	20	3 (15.0)	17 (85.0)	NE (NE, NE)	0.3086 (0.0515, 1.8474)	0.1756	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.7080
Positive	331	19 (5.7)	312 (94.3)	NE (NE, NE)	155	21 (13.5)	134 (86.5)	NE (NE, NE)	0.3345 (0.1778, 0.6292)	0.0004	
Negative	40	2 (5.0)	38 (95.0)	NE (NE, NE)	17	3 (17.6)	14 (82.4)	NE (NE, NE)	0.2731 (0.0456, 1.6349)	0.1303	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0462
HER2 IHC 1+	214	23 (10.7)	191 (89.3)	NE (NE, NE)	100	8 (8.0)	92 (92.0)	NE (NE, NE)	0.9831 (0.4326, 2.2341) 0.9675	0.9674	
HER2 IHC 2+/ISH Negative	157	18 (11.5)	139 (88.5)	NE (NE, NE)	72	1 (1.4)	71 (98.6)	NE (NE, NE)	6.6256 (0.8795, 49.9126) 0.0665	0.0342	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.1947
1	220	15 (6.8)	205 (93.2)	NE (NE, NE)	94	5 (5.3)	89 (94.7)	NE (NE, NE)	1.0672 (0.3841, 2.9648) 0.9007	0.9005	
>=2	150	26 (17.3)	124 (82.7)	NE (NE, NE)	78	4 (5.1)	74 (94.9)	NE (NE, NE)	2.3793 (0.8180, 6.9200) 0.1116	0.1014	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.9122
Yes	233	24 (10.3)	209 (89.7)	NE (NE, NE)	112	5 (4.5)	107 (95.5)	NE (NE, NE)	1.6422 (0.6168, 4.3724) 0.3208	0.3164	
No	98	11 (11.2)	87 (88.8)	NE (NE, NE)	43	2 (4.7)	41 (95.3)	NE (NE, NE)	2.0485 (0.4502, 9.3218) 0.3536	0.3436	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2381
<65	289	30 (10.4)	259 (89.6)	NE (NE, NE)	126	4 (3.2)	122 (96.8)	NE (NE, NE)	2.4271 (0.8464, 6.9605) 0.0990	0.0887	
>=65	82	11 (13.4)	71 (86.6)	NE (NE, NE)	46	5 (10.9)	41 (89.1)	NE (NE, NE)	1.0032 (0.3432, 2.9322) 0.9954	0.9966	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4090
<75	357	40 (11.2)	317 (88.8)	NE (NE, NE)	163	9 (5.5)	154 (94.5)	NE (NE, NE)	1.5346 (0.7373, 3.1941) 0.2521	0.2483	
>=75	14	1 (7.1)	13 (92.9)	NE (5.9, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9985	0.4561	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.9789
White	175	18 (10.3)	157 (89.7)	NE (NE, NE)	85	4 (4.7)	81 (95.3)	NE (NE, NE)	1.5397 (0.5128, 4.6227) 0.4416	0.4380	
Non-White	196	23 (11.7)	173 (88.3)	NE (NE, NE)	86	5 (5.8)	81 (94.2)	NE (NE, NE)	1.6436 (0.6187, 4.3660) 0.3189	0.3141	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.9980
Asia	147	15 (10.2)	132 (89.8)	NE (NE, NE)	63	3 (4.8)	60 (95.2)	NE (NE, NE)	1.7848 (0.5105, 6.2396) 0.3643	0.3576	
North America	58	5 (8.6)	53 (91.4)	NE (NE, NE)	28	1 (3.6)	27 (96.4)	NE (NE, NE)	0.9070 (0.0996, 8.2574) 0.9309	0.9309	
Europe + Israel	166	21 (12.7)	145 (87.3)	NE (NE, NE)	81	5 (6.2)	76 (93.8)	NE (NE, NE)	1.6436 (0.6138, 4.4007) 0.3228	0.3181	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.1562
0	199	19 (9.5)	180 (90.5)	NE (NE, NE)	95	2 (2.1)	93 (97.9)	NE (NE, NE)	3.4429 (0.7947, 14.9154) 0.0984	0.0788	
1	172	22 (12.8)	150 (87.2)	NE (NE, NE)	77	7 (9.1)	70 (90.9)	NE (NE, NE)	1.0526 (0.4418, 2.5077) 0.9078	0.9070	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.8119
0	60	11 (18.3)	49 (81.7)	NE (NE, NE)	31	3 (9.7)	28 (90.3)	NE (NE, NE)	1.3295 (0.3601, 4.9077) 0.6691	0.6694	
1	107	9 (8.4)	98 (91.6)	NE (NE, NE)	48	3 (6.3)	45 (93.8)	NE (NE, NE)	1.2335 (0.3324, 4.5771) 0.7538	0.7542	
2	114	11 (9.6)	103 (90.4)	NE (NE, NE)	50	1 (2.0)	49 (98.0)	NE (NE, NE)	3.1545 (0.3974, 25.0420) 0.2771	0.2519	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	10 (11.1)	80 (88.9)	NE (NE, NE)	43	2 (4.7)	41 (95.3)	NE (NE, NE)	1.7758 (0.3812, 8.2717) 0.4645	0.4586	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.1193
PD	173	16 (9.2)	157 (90.8)	NE (NE, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	2.8791 (0.6568, 12.6200)	0.1424	
PR	48	6 (12.5)	42 (87.5)	NE (NE, NE)	21	4 (19.0)	17 (81.0)	NE (NE, NE)	0.5363 (0.1487, 1.9341)	0.3336	
SD	82	10 (12.2)	72 (87.8)	NE (NE, NE)	54	2 (3.7)	52 (96.3)	NE (NE, NE)	2.5266 (0.5445, 11.7240)	0.2203	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.2524
Yes	37	4 (10.8)	33 (89.2)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9959	0.2369	
No	334	37 (11.1)	297 (88.9)	NE (NE, NE)	159	9 (5.7)	150 (94.3)	NE (NE, NE)	1.4512 (0.6932, 3.0384) 0.3232	0.3205	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.3227
Yes	24	3 (12.5)	21 (87.5)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9966	0.3351	
No	347	38 (11.0)	309 (89.0)	NE (NE, NE)	165	9 (5.5)	156 (94.5)	NE (NE, NE)	1.4779 (0.7073, 3.0881) 0.2988	0.2957	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.8300
Normal Function	201	20 (10.0)	181 (90.0)	NE (NE, NE)	80	5 (6.3)	75 (93.8)	NE (NE, NE)	1.1567 (0.4261, 3.1399) 0.7751	0.7746	
Mild Impairment	123	14 (11.4)	109 (88.6)	NE (NE, NE)	65	3 (4.6)	62 (95.4)	NE (NE, NE)	1.8921 (0.5345, 6.6983) 0.3228	0.3153	
Moderate Impairment	41	4 (9.8)	37 (90.2)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	1.7867 (0.1978, 16.1431) 0.6053	0.6003	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.2202
Normal Function	170	16 (9.4)	154 (90.6)	NE (NE, NE)	88	6 (6.8)	82 (93.2)	NE (NE, NE)	1.1032 (0.4264, 2.8542) 0.8395	0.8396	
Mild Impairment	194	24 (12.4)	170 (87.6)	NE (NE, NE)	82	3 (3.7)	79 (96.3)	NE (NE, NE)	2.4550 (0.7301, 8.2556) 0.1466	0.1338	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.4237
Yes	331	37 (11.2)	294 (88.8)	NE (NE, NE)	146	7 (4.8)	139 (95.2)	NE (NE, NE)	1.8442 (0.8164, 4.1657) 0.1410	0.1352	
No	40	4 (10.0)	36 (90.0)	NE (NE, NE)	26	2 (7.7)	24 (92.3)	NE (NE, NE)	0.6537 (0.1015, 4.2113) 0.6547	0.6527	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.3043
Positive	329	34 (10.3)	295 (89.7)	NE (NE, NE)	152	6 (3.9)	146 (96.1)	NE (NE, NE)	1.9730 (0.8205, 4.7443)	0.1220	
Negative	42	7 (16.7)	35 (83.3)	NE (NE, NE)	20	3 (15.0)	17 (85.0)	NE (NE, NE)	0.8642 (0.2140, 3.4899)	0.8375	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.4982
Positive	331	35 (10.6)	296 (89.4)	NE (NE, NE)	155	7 (4.5)	148 (95.5)	NE (NE, NE)	1.7692 (0.7784, 4.0211)	0.1677	
Negative	40	6 (15.0)	34 (85.0)	NE (NE, NE)	17	2 (11.8)	15 (88.2)	NE (NE, NE)	0.9376 (0.1791, 4.9078)	0.9392	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.4882
HER2 IHC 1+	214	9 (4.2)	205 (95.8)	NE (NE, NE)	100	2 (2.0)	98 (98.0)	NE (NE, NE)	1.8398 (0.3937, 8.5973) 0.4383	0.4309	
HER2 IHC 2+/ISH Negative	157	11 (7.0)	146 (93.0)	NE (NE, NE)	72	1 (1.4)	71 (98.6)	NE (NE, NE)	3.5362 (0.4493, 27.8348) 0.2302	0.2010	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.9451
1	220	7 (3.2)	213 (96.8)	NE (NE, NE)	94	1 (1.1)	93 (98.9)	NE (NE, NE)	2.6003 (0.3174, 21.3023) 0.3732	0.3545	
>=2	150	13 (8.7)	137 (91.3)	NE (NE, NE)	78	2 (2.6)	76 (97.4)	NE (NE, NE)	2.4030 (0.5311, 10.8729) 0.2550	0.2406	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.3474
Yes	233	10 (4.3)	223 (95.7)	NE (NE, NE)	112	1 (0.9)	111 (99.1)	NE (NE, NE)	3.7160 (0.4701, 29.3752) 0.2134	0.1822	
No	98	6 (6.1)	92 (93.9)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9953	0.1719	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9592
<65	289	15 (5.2)	274 (94.8)	NE (NE, NE)	126	2 (1.6)	124 (98.4)	NE (NE, NE)	2.7144 (0.6162, 11.9563) 0.1868	0.1693	
>=65	82	5 (6.1)	77 (93.9)	NE (NE, NE)	46	1 (2.2)	45 (97.8)	NE (NE, NE)	1.7387 (0.1939, 15.5872) 0.6211	0.6170	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9998
<75	357	20 (5.6)	337 (94.4)	NE (NE, NE)	163	3 (1.8)	160 (98.2)	NE (NE, NE)	2.3377 (0.6865, 7.9609) 0.1744	0.1619	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.7843
White	175	8 (4.6)	167 (95.4)	NE (NE, NE)	85	1 (1.2)	84 (98.8)	NE (NE, NE)	2.8479 (0.3505, 23.1378) 0.3275	0.3062	
Non-White	196	12 (6.1)	184 (93.9)	NE (NE, NE)	86	2 (2.3)	84 (97.7)	NE (NE, NE)	2.1518 (0.4750, 9.7484) 0.3202	0.3084	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.3870
Asia	147	9 (6.1)	138 (93.9)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (NE, NE)	3.2879 (0.4119, 26.2469) 0.2614	0.2337	
North America	58	1 (1.7)	57 (98.3)	NE (NE, NE)	28	1 (3.6)	27 (96.4)	NE (NE, NE)	0.3556 (0.0222, 5.6872) 0.4648	0.4449	
Europe + Israel	166	10 (6.0)	156 (94.0)	NE (NE, NE)	81	1 (1.2)	80 (98.8)	NE (NE, NE)	3.5759 (0.4511, 28.3488) 0.2277	0.1980	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.5780
0	199	10 (5.0)	189 (95.0)	NE (NE, NE)	95	1 (1.1)	94 (98.9)	NE (NE, NE)	3.6642 (0.4631, 28.9926) 0.2185	0.1879	
1	172	10 (5.8)	162 (94.2)	NE (NE, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	1.7583 (0.3780, 8.1796) 0.4718	0.4656	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.3315
0	60	6 (10.0)	54 (90.0)	NE (NE, NE)	31	2 (6.5)	29 (93.5)	NE (NE, NE)	1.1897 (0.2351, 6.0220) 0.8337	0.8335	
1	107	4 (3.7)	103 (96.3)	NE (NE, NE)	48	1 (2.1)	47 (97.9)	NE (NE, NE)	1.5814 (0.1752, 14.2764) 0.6831	0.6814	
2	114	5 (4.4)	109 (95.6)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	NE (NE, NE) 0.9960	0.2352	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	5 (5.6)	85 (94.4)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9954	0.1635	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.4773
PD	173	6 (3.5)	167 (96.5)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	2.1309 (0.2510, 18.0911)	0.4780	
PR	48	4 (8.3)	44 (91.7)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	NE (NE, NE)	0.1887	
SD	82	5 (6.1)	77 (93.9)	NE (NE, NE)	54	2 (3.7)	52 (96.3)	NE (NE, NE)	1.2208 (0.2299, 6.4818)	0.8138	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.3958
Yes	37	3 (8.1)	34 (91.9)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9965	0.3090	
No	334	17 (5.1)	317 (94.9)	NE (NE, NE)	159	3 (1.9)	156 (98.1)	NE (NE, NE)	2.0193 (0.5834, 6.9895) 0.2673	0.2577	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.5010
Yes	24	2 (8.3)	22 (91.7)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9973	0.4401	
No	347	18 (5.2)	329 (94.8)	NE (NE, NE)	165	3 (1.8)	162 (98.2)	NE (NE, NE)	2.1328 (0.6200, 7.3370) 0.2295	0.2188	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.2098
Normal Function	201	12 (6.0)	189 (94.0)	NE (NE, NE)	80	2 (2.5)	78 (97.5)	NE (NE, NE)	1.8566 (0.4087, 8.4340) 0.4230	0.4160	
Mild Impairment	123	6 (4.9)	117 (95.1)	NE (NE, NE)	65	0	65 (100)	NE (NE, NE)	NE (NE, NE) 0.9948	0.1108	
Moderate Impairment	41	1 (2.4)	40 (97.6)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	0.4103 (0.0248, 6.7870) 0.5338	0.5210	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.0407
Normal Function	170	8 (4.7)	162 (95.3)	NE (NE, NE)	88	3 (3.4)	85 (96.6)	NE (NE, NE)	0.9471 (0.2434, 3.6860) 0.9375	0.9378	
Mild Impairment	194	11 (5.7)	183 (94.3)	NE (NE, NE)	82	0	82 (100)	NE (NE, NE)	NE (NE, NE) 0.9933	0.0473	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.0880
Yes	331	17 (5.1)	314 (94.9)	NE (NE, NE)	146	1 (0.7)	145 (99.3)	NE (NE, NE)	6.2595 (0.8288, 47.2714) 0.0754	0.0418	
No	40	3 (7.5)	37 (92.5)	NE (NE, NE)	26	2 (7.7)	24 (92.3)	NE (NE, NE)	0.3833 (0.0483, 3.0416) 0.3642	0.3509	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.0073
Positive	329	15 (4.6)	314 (95.4)	NE (NE, NE)	152	0	152 (100)	NE (NE, NE)	NE (NE, NE) 0.9924	0.0246	
Negative	42	5 (11.9)	37 (88.1)	NE (NE, NE)	20	3 (15.0)	17 (85.0)	NE (NE, NE)	0.7022 (0.1656, 2.9781) 0.6315	0.6298	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.0882
Positive	331	16 (4.8)	315 (95.2)	NE (NE, NE)	155	1 (0.6)	154 (99.4)	NE (NE, NE)	5.5558 (0.7295, 42.3116)	0.0627	
Negative	40	4 (10.0)	36 (90.0)	NE (NE, NE)	17	2 (11.8)	15 (88.2)	NE (NE, NE)	0.7312 (0.1309, 4.0841)	0.7203	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
HER2 status											
HER2 IHC 1+	214	22 (10.3)	192 (89.7)	NE (NE, NE)	100	4 (4.0)	96 (96.0)	NE (NE, NE)	2.0743 (0.7078, 6.0794) 0.1835	0.1745	0.9757
HER2 IHC 2+/ISH Negative	157	17 (10.8)	140 (89.2)	NE (NE, NE)	72	3 (4.2)	69 (95.8)	NE (NE, NE)	2.2359 (0.6506, 7.6843) 0.2015	0.1903	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting									0.3575
1	220	20 (9.1)	200 (90.9) NE (NE, NE)	94	2 (2.1)	92 (97.9) NE (NE, NE)	3.5339 (0.8210, 15.2108) 0.0900	0.0706	
>=2	150	19 (12.7)	131 (87.3) NE (NE, NE)	78	5 (6.4)	73 (93.6) NE (NE, NE)	1.6987 (0.6289, 4.5887) 0.2960	0.2913	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Prior CDK4/6											
Yes	233	24 (10.3)	209 (89.7)	NE (NE, NE)	112	3 (2.7)	109 (97.3)	NE (NE, NE)	3.0937 (0.9224, 10.3765) 0.0674	0.0542	0.3871
No	98	12 (12.2)	86 (87.8)	NE (NE, NE)	43	3 (7.0)	40 (93.0)	NE (NE, NE)	1.6058 (0.4524, 5.7003) 0.4637	0.4596	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3388
<65	289	27 (9.3)	262 (90.7)	NE (NE, NE)	126	3 (2.4)	123 (97.6)	NE (NE, NE)	3.3912 (1.0236, 11.2350) 0.0457	0.0338	
>=65	82	12 (14.6)	70 (85.4)	NE (NE, NE)	46	4 (8.7)	42 (91.3)	NE (NE, NE)	1.3305 (0.4219, 4.1956) 0.6261	0.6249	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1534
<75	357	35 (9.8)	322 (90.2)	NE (NE, NE)	163	4 (2.5)	159 (97.5)	NE (NE, NE)	3.4207 (1.2101, 9.6700) 0.0204	0.0136	
>=75	14	4 (28.6)	10 (71.4)	14.7 (5.5, NE)	9	3 (33.3)	6 (66.7)	NE (0.5, NE)	0.7637 (0.1702, 3.4261) 0.7248	0.7240	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Race										0.3550
White	175	23 (13.1)	152 (86.9)	NE (NE, NE)	85	3 (3.5)	82 (96.5)	NE (NE, NE)	2.9432 (0.8758, 9.8908) 0.0809	0.0675
Non-White	196	16 (8.2)	180 (91.8)	NE (NE, NE)	86	4 (4.7)	82 (95.3)	NE (NE, NE)	1.5811 (0.5258, 4.7542) 0.4147	0.4113

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.0831
Asia	147	11 (7.5)	136 (92.5)	NE (NE, NE)	63	4 (6.3)	59 (93.7)	NE (NE, NE)	0.9690 (0.3051, 3.0772) 0.9574	0.9577	
North America	58	9 (15.5)	49 (84.5)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9940	0.0681	
Europe + Israel	166	19 (11.4)	147 (88.6)	NE (NE, NE)	81	3 (3.7)	78 (96.3)	NE (NE, NE)	2.6907 (0.7919, 9.1425) 0.1127	0.0991	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	199	16 (8.0)	183 (92.0)	NE (NE, NE)	95	2 (2.1)	93 (97.9)	NE (NE, NE)	2.6594 (0.6046, 11.6971)	0.1787	0.5710
1	172	23 (13.4)	149 (86.6)	NE (NE, NE)	77	5 (6.5)	72 (93.5)	NE (NE, NE)	1.9400 (0.7333, 5.1325)	0.1748	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1849
0	60	3 (5.0)	57 (95.0)	NE (NE, NE)	31	3 (9.7)	28 (90.3)	NE (NE, NE)	0.3799 (0.0743, 1.9422)	0.2284	
1	107	6 (5.6)	101 (94.4)	NE (NE, NE)	48	1 (2.1)	47 (97.9)	NE (NE, NE)	2.1844 (0.2593, 18.3990)	0.4614	
2	114	23 (20.2)	91 (79.8)	NE (NE, NE)	50	2 (4.0)	48 (96.0)	NE (NE, NE)	4.5018 (1.0552, 19.2066)	0.0260	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 7 (7.8)	83 (92.2)	NE (NE, NE)	43 1 (2.3)	42 (97.7)	NE (NE, NE)	2.5495 (0.3073, 21.1501) 0.3859	0.3690	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.3940
PD	173	20 (11.6)	153 (88.4)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	7.7279 (1.0336, 57.7809) 0.0464	0.0185	
PR	48	6 (12.5)	42 (87.5)	NE (NE, NE)	21	1 (4.8)	20 (95.2)	NE (NE, NE)	2.1374 (0.2554, 17.8899) 0.4835	0.4731	
SD	82	9 (11.0)	73 (89.0)	NE (NE, NE)	54	3 (5.6)	51 (94.4)	NE (NE, NE)	1.4020 (0.3717, 5.2872) 0.6179	0.6162	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.3693
Yes	37	3 (8.1)	34 (91.9)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9964	0.2978	
No	334	36 (10.8)	298 (89.2)	NE (NE, NE)	159	7 (4.4)	152 (95.6)	NE (NE, NE)	2.0065 (0.8870, 4.5388) 0.0945	0.0884	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Baseline CNS metastases											
Yes	24	2 (8.3)	22 (91.7)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9973	0.4401	0.4717
No	347	37 (10.7)	310 (89.3)	NE (NE, NE)	165	7 (4.2)	158 (95.8)	NE (NE, NE)	2.0550 (0.9101, 4.6401) 0.0830	0.0769	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Renal function at baseline										0.0129
Normal Function	201	22 (10.9)	179 (89.1)	NE (NE, NE)	80	0	80 (100)	NE (NE, NE) 0.9907	0.0063	
Mild Impairment	123	11 (8.9)	112 (91.1)	NE (NE, NE)	65	5 (7.7)	60 (92.3)	0.9261 (0.3187, 2.6910) 0.8879	0.8870	
Moderate Impairment	41	6 (14.6)	35 (85.4)	NE (14.7, NE)	23	2 (8.7)	21 (91.3)	1.6002 (0.3222, 7.9481) 0.5654	0.5615	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Hepatic function at baseline											
Normal Function	170	18 (10.6)	152 (89.4)	NE (NE, NE)	88	3 (3.4)	85 (96.6)	NE (NE, NE)	2.7433 (0.8035, 9.3660) 0.1072	0.0933	0.6557
Mild Impairment	194	21 (10.8)	173 (89.2)	NE (NE, NE)	82	4 (4.9)	78 (95.1)	NE (NE, NE)	1.7408 (0.5912, 5.1263) 0.3144	0.3090	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.2765
Yes	331	38 (11.5)	293 (88.5)	NE (NE, NE)	146	6 (4.1)	140 (95.9)	NE (NE, NE)	2.3682 (0.9964, 5.6282) 0.0509	0.0444	
No	40	1 (2.5)	39 (97.5)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	0.6583 (0.0412, 10.5249) 0.7675	0.7658	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.6056
Positive	329	36 (10.9)	293 (89.1)	NE (NE, NE)	152	6 (3.9)	146 (96.1)	NE (NE, NE)	2.3412 (0.9814, 5.5853) 0.0552	0.0484	
Negative	42	3 (7.1)	39 (92.9)	NE (NE, NE)	20	1 (5.0)	19 (95.0)	NE (4.9, NE)	0.8875 (0.0863, 9.1272) 0.9200	0.9200	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 18:47; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_AESEVSOCPT5PER\_2\_SAS.rtf

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.5274
Positive	331	36 (10.9)	295 (89.1)	NE (NE, NE)	155	6 (3.9)	149 (96.1)	NE (NE, NE)	2.3779 (0.9967, 5.6733)	0.0442	
Negative	40	3 (7.5)	37 (92.5)	NE (NE, NE)	17	1 (5.9)	16 (94.1)	NE (4.9, NE)	0.7005 (0.0652, 7.5249)	0.7680	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.7774
HER2 IHC 1+	214	18 (8.4)	196 (91.6)	NE (NE, NE)	100	3 (3.0)	97 (97.0)	NE (NE, NE)	1.6770 (0.4873, 5.7715) 0.4123	0.4075	
HER2 IHC 2+/ISH Negative	157	14 (8.9)	143 (91.1)	NE (NE, NE)	72	3 (4.2)	69 (95.8)	NE (NE, NE)	1.3923 (0.3935, 4.9261) 0.6077	0.6059	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.7415
1	220	14 (6.4)	206 (93.6)	NE (NE, NE)	94	3 (3.2)	91 (96.8)	NE (NE, NE)	1.2187 (0.3447, 4.3084) 0.7588	0.7596	
>=2	150	18 (12.0)	132 (88.0)	NE (NE, NE)	78	3 (3.8)	75 (96.2)	NE (NE, NE)	1.9243 (0.5576, 6.6407) 0.3003	0.2923	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.1152
Yes	233	17 (7.3)	216 (92.7)	NE (NE, NE)	112	1 (0.9)	111 (99.1)	NE (NE, NE)	5.0042 (0.6570, 38.1182) 0.1201	0.0849	
No	98	8 (8.2)	90 (91.8)	NE (NE, NE)	43	3 (7.0)	40 (93.0)	NE (NE, NE)	0.7665 (0.2024, 2.9021) 0.6954	0.6946	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9831
<65	289	24 (8.3)	265 (91.7)	NE (NE, NE)	126	4 (3.2)	122 (96.8)	NE (NE, NE)	1.7140 (0.5881, 4.9955) 0.3235	0.3182	
>=65	82	8 (9.8)	74 (90.2)	NE (NE, NE)	46	2 (4.3)	44 (95.7)	NE (NE, NE)	1.2613 (0.2630, 6.0483) 0.7716	0.7711	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7535
<75	357	30 (8.4)	327 (91.6)	NE (NE, NE)	163	5 (3.1)	158 (96.9)	NE (NE, NE)	1.7332 (0.6649, 4.5184) 0.2606	0.2550	
>=75	14	2 (14.3)	12 (85.7)	NE (5.5, NE)	9	1 (11.1)	8 (88.9)	NE (4.7, NE)	0.9301 (0.0841, 10.2866) 0.9529	0.9528	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.2793
White	175	18 (10.3)	157 (89.7)	NE (NE, NE)	85	2 (2.4)	83 (97.6)	NE (NE, NE)	2.8186 (0.6476, 12.2671) 0.1673	0.1493	
Non-White	196	14 (7.1)	182 (92.9)	NE (NE, NE)	86	4 (4.7)	82 (95.3)	NE (NE, NE)	0.9371 (0.3026, 2.9025) 0.9103	0.9103	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.0441
Asia	147	8 (5.4)	139 (94.6)	NE (NE, NE)	63	4 (6.3)	59 (93.7)	NE (NE, NE)	0.4842 (0.1429, 1.6414) 0.2443	0.2347	
North America	58	9 (15.5)	49 (84.5)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9944	0.1112	
Europe + Israel	166	15 (9.0)	151 (91.0)	NE (NE, NE)	81	2 (2.5)	79 (97.5)	NE (NE, NE)	2.6025 (0.5879, 11.5206) 0.2076	0.1913	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.4801
0	199	11 (5.5)	188 (94.5)	NE (NE, NE)	95	3 (3.2)	92 (96.8)	NE (NE, NE)	0.9670 (0.2647, 3.5324) 0.9595	0.9599	
1	172	21 (12.2)	151 (87.8)	NE (NE, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	2.1207 (0.6244, 7.2026) 0.2282	0.2179	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.0767
0	60	9 (15.0)	51 (85.0)	NE (NE, NE)	31	3 (9.7)	28 (90.3)	NE (4.7, NE)	0.8457 (0.2228, 3.2093) 0.8054	0.8052	
1	107	7 (6.5)	100 (93.5)	NE (NE, NE)	48	1 (2.1)	47 (97.9)	NE (NE, NE)	2.7840 (0.3411, 22.7207) 0.3391	0.3183	
2	114	13 (11.4)	101 (88.6)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	NE (NE, NE) 0.9940	0.0959	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam

Run date: 13SEP2022 – 18:47; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_AESEVSOCPT5PER\_2\_SAS.rtf

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	3 (3.3)	87 (96.7)	NE (NE, NE)	43	2 (4.7)	41 (95.3)	NE (NE, NE)	0.3647 (0.0572, 2.3252) 0.2859	0.2686	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.2168
PD	173	15 (8.7)	158 (91.3)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	3.8294 (0.4983, 29.4265)	0.1654	
PR	48	3 (6.3)	45 (93.8)	NE (NE, NE)	21	1 (4.8)	20 (95.2)	NE (NE, NE)	0.1969 (0.0665, 7.2484)	0.7596	
SD	82	4 (4.9)	78 (95.1)	NE (NE, NE)	54	3 (5.6)	51 (94.4)	NE (NE, NE)	0.6445 (0.1424, 2.9168)	0.5656	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.1616
Yes	37	1 (2.7)	36 (97.3)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	0.2265 (0.0134, 3.8135) 0.3026	0.2626	
No	334	31 (9.3)	303 (90.7)	NE (NE, NE)	159	5 (3.1)	154 (96.9)	NE (NE, NE)	1.8486 (0.7114, 4.8036) 0.2073	0.2006	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0371
Yes	24	0	24 (100)	NE (NE, NE)	7	1 (14.3)	6 (85.7)	NE (0.8, NE)	0.0000 (0.0000, ) 0.9982	0.0699	
No	347	32 (9.2)	315 (90.8)	NE (NE, NE)	165	5 (3.0)	160 (97.0)	NE (NE, NE)	1.8642 (0.7188, 4.8344) 0.2002	0.1934	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.2774
Normal Function	201	17 (8.5)	184 (91.5)	NE (NE, NE)	80	3 (3.8)	77 (96.3)	NE (NE, NE)	1.3573 (0.3906, 4.7165) 0.6307	0.6297	
Mild Impairment	123	10 (8.1)	113 (91.9)	NE (NE, NE)	65	3 (4.6)	62 (95.4)	NE (NE, NE)	1.0880 (0.2924, 4.0484) 0.8999	0.8999	
Moderate Impairment	41	4 (9.8)	37 (90.2)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9957	0.1885	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.6291
Normal Function	170	15 (8.8)	155 (91.2)	NE (NE, NE)	88	4 (4.5)	84 (95.5)	NE (NE, NE)	0.9517 (0.3118, 2.9053) 0.9307	0.9301	
Mild Impairment	194	15 (7.7)	179 (92.3)	NE (NE, NE)	82	2 (2.4)	80 (97.6)	NE (NE, NE)	2.3422 (0.5312, 10.3275) 0.2609	0.2469	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.8616
Yes	331	28 (8.5)	303 (91.5)	NE (NE, NE)	146	5 (3.4)	141 (96.6)	NE (NE, NE)	1.6564 (0.6335, 4.3306) 0.3034	0.2988	
No	40	4 (10.0)	36 (90.0)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	0.8814 (0.0943, 8.2396) 0.9119	0.9118	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.1400
Positive	329	25 (7.6)	304 (92.4)	NE (NE, NE)	152	3 (2.0)	149 (98.0)	NE (NE, NE)	2.2848 (0.6832, 7.6406) 0.1797	0.1680	
Negative	42	7 (16.7)	35 (83.3)	NE (NE, NE)	20	3 (15.0)	17 (85.0)	NE (4.7, NE)	0.7932 (0.1955, 3.2182) 0.7457	0.7452	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.2724
Positive	331	26 (7.9)	305 (92.1)	NE (NE, NE)	155	4 (2.6)	151 (97.4)	NE (NE, NE)	1.8725 (0.6468, 5.4213)	0.2475	0.2402
Negative	40	6 (15.0)	34 (85.0)	NE (NE, NE)	17	2 (11.8)	15 (88.2)	NE (4.7, NE)	0.7646 (0.1437, 4.0683)	0.7530	0.7524

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.7968
HER2 IHC 1+	214	17 (7.9)	197 (92.1)	NE (NE, NE)	100	4 (4.0)	96 (96.0)	NE (NE, NE)	1.4884 (0.4930, 4.4937) 0.4806	0.4783	
HER2 IHC 2+/ISH Negative	157	14 (8.9)	143 (91.1)	NE (NE, NE)	72	4 (5.6)	68 (94.4)	NE (NE, NE)	1.2864 (0.4192, 3.9479) 0.6598	0.6602	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 18:47; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_AESEVSOCPT5PER\_2\_SAS.rtf

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.3545
1	220	15 (6.8)	205 (93.2)	NE (NE, NE)	94	5 (5.3)	89 (94.7)	NE (NE, NE)	0.9233 (0.3296, 2.5863) 0.8793	0.8778	
>=2	150	16 (10.7)	134 (89.3)	NE (NE, NE)	78	3 (3.8)	75 (96.2)	NE (NE, NE)	2.3082 (0.6663, 7.9961) 0.1870	0.1749	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.0865
Yes	233	22 (9.4)	211 (90.6)	NE (NE, NE)	112	6 (5.4)	106 (94.6)	NE (NE, NE)	1.3563 (0.5430, 3.3878) 0.5141	0.5135	
No	98	7 (7.1)	91 (92.9)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9948	0.1390	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9698
<65	289	22 (7.6)	267 (92.4)	NE (NE, NE)	126	5 (4.0)	121 (96.0)	NE (NE, NE)	1.5507 (0.5825, 4.1286) 0.3798	0.3756	
>=65	82	9 (11.0)	73 (89.0)	NE (NE, NE)	46	3 (6.5)	43 (93.5)	NE (NE, NE)	1.2435 (0.3303, 4.6812) 0.7472	0.7479	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3753
<75	357	30 (8.4)	327 (91.6)	NE (NE, NE)	163	8 (4.9)	155 (95.1)	NE (NE, NE)	1.3005 (0.5896, 2.8686) 0.5150	0.5143	
>=75	14	1 (7.1)	13 (92.9)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9985	0.4142	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.3195
White	175	17 (9.7)	158 (90.3)	NE (NE, NE)	85	6 (7.1)	79 (92.9)	NE (NE, NE)	1.0169 (0.3947, 2.6204) 0.9723	0.9730	
Non-White	196	14 (7.1)	182 (92.9)	NE (NE, NE)	86	2 (2.3)	84 (97.7)	NE (NE, NE)	2.4710 (0.5559, 10.9829) 0.2346	0.2196	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.3614
Asia	147	12 (8.2)	135 (91.8)	NE (NE, NE)	63	2 (3.2)	61 (96.8)	NE (NE, NE)	2.0739 (0.4588, 9.3735) 0.3433	0.3337	
North America	58	3 (5.2)	55 (94.8)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9962	0.2467	
Europe + Israel	166	16 (9.6)	150 (90.4)	NE (NE, NE)	81	6 (7.4)	75 (92.6)	NE (NE, NE)	0.9622 (0.3707, 2.4971) 0.9368	0.9355	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.3532
0	199	13 (6.5)	186 (93.5)	NE (NE, NE)	95	2 (2.1)	93 (97.9)	NE (NE, NE)	2.5414 (0.5692, 11.3476) 0.2218	0.2059	
1	172	18 (10.5)	154 (89.5)	NE (NE, NE)	77	6 (7.8)	71 (92.2)	NE (NE, NE)	0.9852 (0.3835, 2.5307) 0.9753	0.9749	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1037
0	60	5 (8.3)	55 (91.7)	NE (NE, NE)	31	2 (6.5)	29 (93.5)	NE (NE, NE)	1.0178 (0.1902, 5.4470) 0.9836	0.9835	
1	107	10 (9.3)	97 (90.7)	NE (NE, NE)	48	3 (6.3)	45 (93.8)	NE (NE, NE)	1.2432 (0.3392, 4.5566) 0.7425	0.7436	
2	114	11 (9.6)	103 (90.4)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	NE (NE, NE) 0.9932	0.0443	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	5 (5.6)	85 (94.4)	NE (NE, NE)	43	3 (7.0)	40 (93.0)	NE (NE, NE)	0.5271 (0.1199, 2.3172) 0.3966	0.3898	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.4183
PD	173	11 (6.4)	162 (93.6)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	3.7915 (0.4846, 29.6667) 0.2042	0.1726	
PR	48	5 (10.4)	43 (89.6)	NE (NE, NE)	21	1 (4.8)	20 (95.2)	NE (NE, NE)	1.5911 (0.1822, 13.8913) 0.6744	0.6717	
SD	82	9 (11.0)	73 (89.0)	NE (NE, NE)	54	5 (9.3)	49 (90.7)	NE (NE, NE)	0.9026 (0.2966, 2.7467) 0.8567	0.8571	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Run date: 13SEP2022 – 18:47; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_AESEVSOCPT5PER\_2\_SAS.rtf

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.0429
Yes	37	0	37 (100)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	0.0000 (0.0000, ) 0.9980	0.0916	
No	334	31 (9.3)	303 (90.7)	NE (NE, NE)	159	7 (4.4)	152 (95.6)	NE (NE, NE)	1.6479 (0.7196, 3.7735) 0.2374	0.2331	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0381
Yes	24	0	24 (100)	NE (NE, NE)	7	1 (14.3)	6 (85.7)	NE (0.1, NE)	0.0000 (0.0000, ) 0.9983	0.0641	
No	347	31 (8.9)	316 (91.1)	NE (NE, NE)	165	7 (4.2)	158 (95.8)	NE (NE, NE)	1.6285 (0.7109, 3.7306) 0.2489	0.2448	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.9812
Normal Function	201	13 (6.5)	188 (93.5)	NE (NE, NE)	80	3 (3.8)	77 (96.3)	NE (NE, NE)	1.4825 (0.4200, 5.2329) 0.5406	0.5375	
Mild Impairment	123	12 (9.8)	111 (90.2)	NE (NE, NE)	65	3 (4.6)	62 (95.4)	NE (NE, NE)	1.3108 (0.3562, 4.8238) 0.6839	0.6830	
Moderate Impairment	41	6 (14.6)	35 (85.4)	NE (NE, NE)	23	2 (8.7)	21 (91.3)	NE (NE, NE)	1.5080 (0.3035, 7.4914) 0.6155	0.6070	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.7277
Normal Function	170	12 (7.1)	158 (92.9)	NE (NE, NE)	88	3 (3.4)	85 (96.6)	NE (NE, NE)	1.3023 (0.3571, 4.7490) 0.6891	0.6870	
Mild Impairment	194	18 (9.3)	176 (90.7)	NE (NE, NE)	82	5 (6.1)	77 (93.9)	NE (NE, NE)	1.2969 (0.4788, 3.5131) 0.6091	0.6095	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.2111
Yes	331	29 (8.8)	302 (91.2)	NE (NE, NE)	146	6 (4.1)	140 (95.9)	NE (NE, NE)	1.6984 (0.7002, 4.1194) 0.2413	0.2362	
No	40	2 (5.0)	38 (95.0)	NE (NE, NE)	26	2 (7.7)	24 (92.3)	NE (NE, NE)	0.3999 (0.0465, 3.4374) 0.4037	0.3903	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.1628
Positive	329	29 (8.8)	300 (91.2)	NE (NE, NE)	152	6 (3.9)	146 (96.1)	NE (NE, NE)	1.6928 (0.6967, 4.1131) 0.2452	0.2402	
Negative	42	2 (4.8)	40 (95.2)	NE (NE, NE)	20	2 (10.0)	18 (90.0)	NE (NE, NE)	0.4786 (0.0674, 3.3978) 0.4612	0.4510	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.1223
Positive	331	29 (8.8)	302 (91.2)	NE (NE, NE)	155	6 (3.9)	149 (96.1)	NE (NE, NE)	1.7204 (0.7080, 4.1807)	0.2258	
Negative	40	2 (5.0)	38 (95.0)	NE (NE, NE)	17	2 (11.8)	15 (88.2)	NE (NE, NE)	0.2310 (0.0600, 3.0237)	0.4259	0.3789

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.4035
HER2 IHC 1+	214	9 (4.2)	205 (95.8)	NE (NE, NE)	100	5 (5.0)	95 (95.0)	NE (NE, NE)	0.4755 (0.1523, 1.4849) 0.2007	0.1916	
HER2 IHC 2+/ISH Negative	157	11 (7.0)	146 (93.0)	NE (24.4, NE)	72	3 (4.2)	69 (95.8)	NE (NE, NE)	0.9652 (0.2608, 3.5726) 0.9577	0.9573	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.4687
1	220	7 (3.2)	213 (96.8)	NE (24.4, NE)	94	4 (4.3)	90 (95.7)	NE (NE, NE)	0.4230 (0.1167, 1.5331) 0.1903	0.1782	
>=2	150	13 (8.7)	137 (91.3)	NE (NE, NE)	78	4 (5.1)	74 (94.9)	NE (NE, NE)	0.9084 (0.2863, 2.8816) 0.8704	0.8696	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.1559
Yes	233	13 (5.6)	220 (94.4)	NE (24.4, NE)	112	6 (5.4)	106 (94.6)	NE (NE, NE)	0.5170 (0.1883, 1.4193) 0.2004	0.1930	
No	98	3 (3.1)	95 (96.9)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9971	0.3960	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0797
<65	289	19 (6.6)	270 (93.4)	NE (24.4, NE)	126	5 (4.0)	121 (96.0)	NE (NE, NE)	0.9327 (0.3398, 2.5606) 0.8925	0.8922	
>=65	82	1 (1.2)	81 (98.8)	NE (NE, NE)	46	3 (6.5)	43 (93.5)	NE (NE, NE)	0.1188 (0.0119, 1.1818) 0.0691	0.0321	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9998
<75	357	20 (5.6)	337 (94.4)	NE (24.4, NE)	163	8 (4.9)	155 (95.1)	NE (NE, NE)	0.6410 (0.2747, 1.4959)	0.3037	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE)	NE	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.7259
White	175	16 (9.1)	159 (90.9)	24.4 (24.4, NE)	85	6 (7.1)	79 (92.9)	NE (NE, NE)	0.7229 (0.2745, 1.9039) 0.5114	0.5099	
Non-White	196	4 (2.0)	192 (98.0)	NE (NE, NE)	86	2 (2.3)	84 (97.7)	NE (NE, NE)	0.4891 (0.0846, 2.8258) 0.4242	0.4149	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.2973
Asia	147	3 (2.0)	144 (98.0)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (NE, NE)	0.6639 (0.0639, 6.8992) 0.7317	0.7303	
North America	58	8 (13.8)	50 (86.2)	NE (NE, NE)	28	1 (3.6)	27 (96.4)	NE (NE, NE)	2.1748 (0.2640, 17.9161) 0.4702	0.4593	
Europe + Israel	166	9 (5.4)	157 (94.6)	24.4 (24.4, NE)	81	6 (7.4)	75 (92.6)	NE (NE, NE)	0.4253 (0.1442, 1.2537) 0.1211	0.1109	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.2797
0	199	4 (2.0)	195 (98.0)	NE (24.4, NE)	95	3 (3.2)	92 (96.8)	NE (NE, NE)	0.2990 (0.0598, 1.4952) 0.1415	0.1192	
1	172	16 (9.3)	156 (90.7)	NE (NE, NE)	77	5 (6.5)	72 (93.5)	NE (NE, NE)	0.8575 (0.3050, 2.4105) 0.7706	0.7709	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.3633
0	60	5 (8.3)	55 (91.7)	NE (18.1, NE)	31	2 (6.5)	29 (93.5)	NE (NE, NE)	0.6869 (0.1237, 3.8142) 0.6677	0.6621	
1	107	5 (4.7)	102 (95.3)	NE (NE, NE)	48	3 (6.3)	45 (93.8)	NE (NE, NE)	0.5431 (0.1287, 2.2918) 0.4060	0.3989	
2	114	8 (7.0)	106 (93.0)	NE (NE, NE)	50	1 (2.0)	49 (98.0)	NE (NE, NE)	1.8430 (0.2227, 15.2547) 0.5707	0.5650	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	2 (2.2)	88 (97.8)	NE (24.4, NE)	43	2 (4.7)	41 (95.3)	NE (NE, NE)	0.2245 (0.0203, 2.4792) 0.2228	0.1818	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.9555
PD	173	12 (6.9)	161 (93.1)	NE (24.4, NE)	77	5 (6.5)	72 (93.5)	NE (NE, NE)	0.5349 (0.1771, 1.6151) 0.2671	0.2599	
PR	48	2 (4.2)	46 (95.8)	NE (NE, NE)	21	1 (4.8)	20 (95.2)	NE (NE, NE)	0.6718 (0.0597, 7.5585) 0.7474	0.7460	
SD	82	1 (1.2)	81 (98.8)	NE (NE, NE)	54	1 (1.9)	53 (98.1)	NE (NE, NE)	0.4982 (0.0304, 8.1731) 0.6255	0.6188	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.0976
Yes	37	5 (13.5)	32 (86.5)	24.4 (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9967	0.3833	
No	334	15 (4.5)	319 (95.5)	NE (NE, NE)	159	8 (5.0)	151 (95.0)	NE (NE, NE)	0.5513 (0.2285, 1.3301) 0.1851	0.1793	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.1251
Yes	24	4 (16.7)	20 (83.3)	24.4 (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9968	0.3712	
No	347	16 (4.6)	331 (95.4)	NE (NE, NE)	165	8 (4.8)	157 (95.2)	NE (NE, NE)	0.5552 (0.2317, 1.3308) 0.1871	0.1815	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.7382
Normal Function	201	11 (5.5)	190 (94.5)	NE (24.4, NE)	80	3 (3.8)	77 (96.3)	NE (NE, NE)	0.8835 (0.2376, 3.2854) 0.8534	0.8533	
Mild Impairment	123	6 (4.9)	117 (95.1)	NE (NE, NE)	65	4 (6.2)	61 (93.8)	NE (NE, NE)	0.3625 (0.0936, 1.4033) 0.1417	0.1263	
Moderate Impairment	41	2 (4.9)	39 (95.1)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	0.9064 (0.0815, 10.0846) 0.9363	0.9363	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1520
Normal Function	170	9 (5.3)	161 (94.7)	NE (NE, NE)	88	2 (2.3)	86 (97.7)	NE (NE, NE)	1.5444 (0.3306, 7.2140) 0.5805	0.5780	
Mild Impairment	194	10 (5.2)	184 (94.8)	NE (24.4, NE)	82	6 (7.3)	76 (92.7)	NE (NE, NE)	0.3223 (0.1072, 0.9694) 0.0439	0.0348	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.2245
Yes	331	18 (5.4)	313 (94.6)	NE (24.4, NE)	146	8 (5.5)	138 (94.5)	NE (NE, NE)	0.6184 (0.2635, 1.4514) 0.2696	0.2658	
No	40	2 (5.0)	38 (95.0)	NE (18.1, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9972	0.6225	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.8583
Positive	329	14 (4.3)	315 (95.7)	NE (24.4, NE)	152	6 (3.9)	146 (96.1)	NE (NE, NE)	0.5501 (0.2031, 1.4895)	0.2332	
Negative	42	6 (14.3)	36 (85.7)	NE (NE, NE)	20	2 (10.0)	18 (90.0)	NE (NE, NE)	1.0393 (0.2066, 5.2270)	0.9659	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.7478
Positive	331	15 (4.5)	316 (95.5)	NE (24.4, NE)	155	6 (3.9)	149 (96.1)	NE (NE, NE)	0.6493 (0.2441, 1.7276)	0.3841	
Negative	40	5 (12.5)	35 (87.5)	NE (11.1, NE)	17	2 (11.8)	15 (88.2)	NE (NE, NE)	0.5556 (0.0981, 3.1471)	0.4958	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.6609
HER2 IHC 1+	214	3 (1.4)	211 (98.6)	NE (NE, NE)	100	6 (6.0)	94 (94.0)	NE (NE, NE)	0.1377 (0.0325, 0.5829) 0.0071	0.0021	
HER2 IHC 2+/ISH Negative	157	4 (2.5)	153 (97.5)	NE (NE, NE)	72	5 (6.9)	67 (93.1)	NE (NE, NE)	0.2301 (0.0594, 0.8910) 0.0334	0.0214	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.1303
1	220	3 (1.4)	217 (98.6)	NE (NE, NE)	94	8 (8.5)	86 (91.5)	NE (NE, NE)	0.0947 (0.0239, 0.3751) 0.0008	<0.0001	
>=2	150	4 (2.7)	146 (97.3)	NE (NE, NE)	78	3 (3.8)	75 (96.2)	NE (NE, NE)	0.4381 (0.0927, 2.0712) 0.2977	0.2858	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.4145
Yes	233	3 (1.3)	230 (98.7)	NE (NE, NE)	112	7 (6.3)	105 (93.8)	NE (NE, NE)	0.1346 (0.0333, 0.5432) 0.0048	0.0012	
No	98	3 (3.1)	95 (96.9)	NE (NE, NE)	43	3 (7.0)	40 (93.0)	NE (NE, NE)	0.2802 (0.0546, 1.4377) 0.1273	0.1053	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3938
<65	289	7 (2.4)	282 (97.6)	NE (NE, NE)	126	10 (7.9)	116 (92.1)	NE (NE, NE)	0.1647 (0.0594, 0.4565) 0.0005	0.0001	
>=65	82	0	82 (100)	NE (NE, NE)	46	1 (2.2)	45 (97.8)	NE (NE, NE)	0.0000 (0.0000, ) 0.9976	0.1818	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9993
<75	357	7 (2.0)	350 (98.0)	NE (NE, NE)	163	11 (6.7)	152 (93.3)	NE (NE, NE)	0.1637 (0.0603, 0.4443) 0.0004	<0.0001	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.8757
White	175	4 (2.3)	171 (97.7)	NE (NE, NE)	85	6 (7.1)	79 (92.9)	NE (NE, NE)	0.2225 (0.0609, 0.8127) 0.0230	0.0134	
Non-White	196	3 (1.5)	193 (98.5)	NE (NE, NE)	86	5 (5.8)	81 (94.2)	NE (NE, NE)	0.1241 (0.0270, 0.5711) 0.0074	0.0022	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.0751
Asia	147	2 (1.4)	145 (98.6)	NE (NE, NE)	63	4 (6.3)	59 (93.7)	NE (NE, NE)	0.0899 (0.0144, 0.5596) 0.0098	0.0023	
North America	58	4 (6.9)	54 (93.1)	NE (NE, NE)	28	1 (3.6)	27 (96.4)	NE (5.8, NE)	0.8237 (0.0858, 7.9060) 0.8665	0.8664	
Europe + Israel	166	1 (0.6)	165 (99.4)	NE (NE, NE)	81	6 (7.4)	75 (92.6)	NE (NE, NE)	0.0756 (0.0091, 0.6283) 0.0168	0.0019	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.4723
0	199	2 (1.0)	197 (99.0)	NE (NE, NE)	95	5 (5.3)	90 (94.7)	NE (NE, NE)	0.1175 (0.0220, 0.6278) 0.0123	0.0031	
1	172	5 (2.9)	167 (97.1)	NE (NE, NE)	77	6 (7.8)	71 (92.2)	NE (NE, NE)	0.2062 (0.0577, 0.7375) 0.0152	0.0084	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.6533
0	60	1 (1.7)	59 (98.3)	NE (NE, NE)	31	4 (12.9)	27 (87.1)	NE (5.3, NE)	0.0478 (0.0043, 0.5353)	0.0020	
1	107	2 (1.9)	105 (98.1)	NE (NE, NE)	48	3 (6.3)	45 (93.8)	NE (NE, NE)	0.2231 (0.0365, 1.3625)	0.0764	
2	114	3 (2.6)	111 (97.4)	NE (NE, NE)	50	2 (4.0)	48 (96.0)	NE (NE, NE)	0.1042 (0.0760, 2.9640)	0.4153	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	1 (1.1)	89 (98.9)	NE (NE, NE)	43	2 (4.7)	41 (95.3)	NE (5.8, NE)	0.1396 (0.0118, 1.6506) 0.1182	0.0735	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.0269
PD	173	4 (2.3)	169 (97.7)	NE (NE, NE)	77	5 (6.5)	72 (93.5)	NE (NE, NE)	0.2238 (0.0562, 0.8906)	0.0215	
PR	48	2 (4.2)	46 (95.8)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	0.0336 (NE, NE)	0.4997	
SD	82	0	82 (100)	NE (NE, NE)	54	5 (9.3)	49 (90.7)	NE (NE, NE)	0.0000 (0.0000, )	0.0025	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.3798
Yes	37	2 (5.4)	35 (94.6)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	0.4792 (0.0404, 5.6843)	0.5517	
No	334	5 (1.5)	329 (98.5)	NE (NE, NE)	159	10 (6.3)	149 (93.7)	NE (NE, NE)	0.5599 (0.0462, 0.4298)	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0492
Yes	24	2 (8.3)	22 (91.7)	NE (11.6, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9975	0.5045	
No	347	5 (1.4)	342 (98.6)	NE (NE, NE)	165	11 (6.7)	154 (93.3)	NE (NE, NE)	0.1284 (0.0428, 0.3849) 0.0002	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.4705
Normal Function	201	6 (3.0)	195 (97.0)	NE (NE, NE)	80	9 (11.3)	71 (88.8)	NE (NE, NE)	0.1125 (0.0359, 0.3525) 0.0002	<0.0001	
Mild Impairment	123	0	123 (100)	NE (NE, NE)	65	1 (1.5)	64 (98.5)	NE (NE, NE)	0.0000 (0.0000, ) 0.9977	0.1590	
Moderate Impairment	41	1 (2.4)	40 (97.6)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	0.5360 (0.0335, 8.5760) 0.6594	0.6542	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.7584
Normal Function	170	4 (2.4)	166 (97.6)	NE (NE, NE)	88	6 (6.8)	82 (93.2)	NE (NE, NE)	0.2388 (0.0649, 0.8784) 0.0312	0.0203	
Mild Impairment	194	3 (1.5)	191 (98.5)	NE (NE, NE)	82	5 (6.1)	77 (93.9)	NE (NE, NE)	0.1237 (0.0274, 0.5589) 0.0066	0.0017	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1372
Yes	331	6 (1.8)	325 (98.2)	NE (NE, NE)	146	11 (7.5)	135 (92.5)	NE (NE, NE)	0.1523 (0.0543, 0.4271) 0.0003	<0.0001	
No	40	1 (2.5)	39 (97.5)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9984	0.7963	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.2606
Positive	329	5 (1.5)	324 (98.5)	NE (NE, NE)	152	10 (6.6)	142 (93.4)	NE (NE, NE)	0.1371 (0.0451, 0.4166) 0.0005	<0.0001	
Negative	42	2 (4.8)	40 (95.2)	NE (NE, NE)	20	1 (5.0)	19 (95.0)	NE (NE, NE)	0.4939 (0.0309, 7.8964) 0.6179	0.6106	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.7885
Positive	331	6 (1.8)	325 (98.2)	NE (NE, NE)	155	10 (6.5)	145 (93.5)	NE (NE, NE)	0.1742 (0.0610, 0.4972)	0.0003	
Negative	40	1 (2.5)	39 (97.5)	NE (NE, NE)	17	1 (5.9)	16 (94.1)	NE (NE, NE)	0.0011 (0.0000, ) 0.9978	0.1299	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.1644
HER2 IHC 1+	214	0	214 (100)	NE (NE, NE)	100	3 (3.0)	97 (97.0)	NE (NE, NE)	0.0000 (0.0000, ) 0.9965	0.0037	
HER2 IHC 2+/ISH Negative	157	3 (1.9)	154 (98.1)	NE (NE, NE)	72	6 (8.3)	66 (91.7)	NE (NE, NE)	0.1691 (0.0416, 0.6865) 0.0129	0.0050	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.4428
1	220	1 (0.5)	219 (99.5)	NE (NE, NE)	94	5 (5.3)	89 (94.7)	NE (NE, NE)	0.0756 (0.0088, 0.6503)	0.0023	
>=2	150	2 (1.3)	148 (98.7)	NE (NE, NE)	78	4 (5.1)	74 (94.9)	NE (NE, NE)	0.1508 (0.0267, 0.8514)	0.0148	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.8826
Yes	233	2 (0.9)	231 (99.1)	NE (NE, NE)	112	5 (4.5)	107 (95.5)	NE (NE, NE)	0.1537 (0.0294, 0.8033) 0.0265	0.0110	
No	98	1 (1.0)	97 (99.0)	NE (NE, NE)	43	3 (7.0)	40 (93.0)	NE (NE, NE)	0.1211 (0.0125, 1.1727) 0.0684	0.0299	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9340
<65	289	2 (0.7)	287 (99.3)	NE (NE, NE)	126	5 (4.0)	121 (96.0)	NE (NE, NE)	0.1111 (0.0210, 0.5866) 0.0096	0.0020	
>=65	82	1 (1.2)	81 (98.8)	NE (NE, NE)	46	4 (8.7)	42 (91.3)	NE (NE, NE)	0.1283 (0.0143, 1.1486) 0.0663	0.0296	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3511
<75	357	3 (0.8)	354 (99.2)	NE (NE, NE)	163	7 (4.3)	156 (95.7)	NE (NE, NE)	0.1376 (0.0350, 0.5411) 0.0045	0.0010	
>=75	14	0	14 (100)	NE (NE, NE)	9	2 (22.2)	7 (77.8)	NE (0.6, NE)	0.0000 (0.0000, ) 0.9977	0.0800	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.0943
White	175	0	175 (100)	NE (NE, NE)	85	4 (4.7)	81 (95.3)	NE (NE, NE)	0.0000 (0.0000, ) 0.9956	0.0024	
Non-White	196	3 (1.5)	193 (98.5)	NE (NE, NE)	86	5 (5.8)	81 (94.2)	NE (NE, NE)	0.1895 (0.0445, 0.8062) 0.0243	0.0123	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.4416
Asia	147	1 (0.7)	146 (99.3)	NE (NE, NE)	63	5 (7.9)	58 (92.1)	NE (NE, NE)	0.0540 (0.0062, 0.4725) 0.0083	0.0003	
North America	58	0	58 (100)	NE (NE, NE)	28	1 (3.6)	27 (96.4)	NE (NE, NE)	0.0000 (0.0000, ) 0.9977	0.1501	
Europe + Israel	166	2 (1.2)	164 (98.8)	NE (NE, NE)	81	3 (3.7)	78 (96.3)	NE (NE, NE)	0.2860 (0.0476, 1.7184) 0.1712	0.1448	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.6758
0	199	2 (1.0)	197 (99.0)	NE (NE, NE)	95	7 (7.4)	88 (92.6)	NE (NE, NE)	0.0874 (0.0179, 0.4276) 0.0026	0.0002	
1	172	1 (0.6)	171 (99.4)	NE (NE, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	0.2249 (0.0204, 2.4809) 0.2232	0.1821	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.4309
0	60	1 (1.7)	59 (98.3)	NE (NE, NE)	31	2 (6.5)	29 (93.5)	NE (5.7, NE)	0.1379 (0.0119, 1.5993)	0.0687	
1	107	1 (0.9)	106 (99.1)	NE (NE, NE)	48	1 (2.1)	47 (97.9)	NE (NE, NE)	0.3830 (0.0239, 6.1268)	0.4809	
2	114	0	114 (100)	NE (NE, NE)	50	3 (6.0)	47 (94.0)	NE (NE, NE)	0.4974 (0.0000, )	0.0078	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.11.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm -  
 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	1 (1.1)	89 (98.9)	NE (NE, NE)	43	3 (7.0)	40 (93.0)	NE (NE, NE)	0.1089 (0.0107, 1.1078) 0.0610	0.0260	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.4942
PD	173	2 (1.2)	171 (98.8)	NE (NE, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	0.3874 (0.0540, 2.7765)	0.3277	
PR	48	0	48 (100)	NE (NE, NE)	21	1 (4.8)	20 (95.2)	NE (5.7, NE)	0.3453 (0.0000, )	0.0065	
SD	82	1 (1.2)	81 (98.8)	NE (NE, NE)	54	4 (7.4)	50 (92.6)	NE (NE, NE)	0.1268 (0.0140, 1.1517)	0.0308	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											NE
Yes	37	0	37 (100)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE)		
No	334	3 (0.9)	331 (99.1)	NE (NE, NE)	159	9 (5.7)	150 (94.3)	NE (NE, NE)	0.1190 (0.0318, 0.4452)	0.0002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.1079
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9982	0.6276	
No	347	2 (0.6)	345 (99.4)	NE (NE, NE)	165	9 (5.5)	156 (94.5)	NE (NE, NE)	0.0814 (0.0174, 0.3808) 0.0014	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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 Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.3192
Normal Function	201	2 (1.0)	199 (99.0)	NE (NE, NE)	80	2 (2.5)	78 (97.5)	NE (NE, NE)	0.2526 (0.0349, 1.8307) 0.1733	0.1427	
Mild Impairment	123	1 (0.8)	122 (99.2)	NE (NE, NE)	65	4 (6.2)	61 (93.8)	NE (NE, NE)	0.1011 (0.0109, 0.9344) 0.0434	0.0144	
Moderate Impairment	41	0	41 (100)	NE (NE, NE)	23	3 (13.0)	20 (87.0)	NE (NE, NE)	0.0000 (0.0000, ) 0.9959	0.0140	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.4030
Normal Function	170	1 (0.6)	169 (99.4)	NE (NE, NE)	88	6 (6.8)	82 (93.2)	NE (NE, NE)	0.0581 (0.0069, 0.4890) 0.0088	0.0004	
Mild Impairment	194	2 (1.0)	192 (99.0)	NE (NE, NE)	82	3 (3.7)	79 (96.3)	NE (NE, NE)	0.2484 (0.0412, 1.4958) 0.1284	0.1002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.3119
Yes	331	3 (0.9)	328 (99.1)	NE (NE, NE)	146	7 (4.8)	139 (95.2)	NE (NE, NE)	0.1492 (0.0382, 0.5829)	0.0016	
No	40	0	40 (100)	NE (NE, NE)	26	2 (7.7)	24 (92.3)	NE (5.7, NE)	0.0000 (0.0000, )	0.0255	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.4468
Positive	329	3 (0.9)	326 (99.1)	NE (NE, NE)	152	8 (5.3)	144 (94.7)	NE (NE, NE)	0.1372 (0.0361, 0.5221)	0.0007	
Negative	42	0	42 (100)	NE (NE, NE)	20	1 (5.0)	19 (95.0)	NE (5.7, NE)	0.0000 (0.0000, ) 0.9987	0.0190	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Skin and subcutaneous tissue disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.4090
Positive	331	3 (0.9)	328 (99.1)	NE (NE, NE)	155	8 (5.2)	147 (94.8)	NE (NE, NE)	0.1399 (0.0368, 0.5320)	0.0008	
Negative	40	0	40 (100)	NE (NE, NE)	17	1 (5.9)	16 (94.1)	NE (5.7, NE)	0.0000 (0.0000, ) 0.9983	0.0068	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

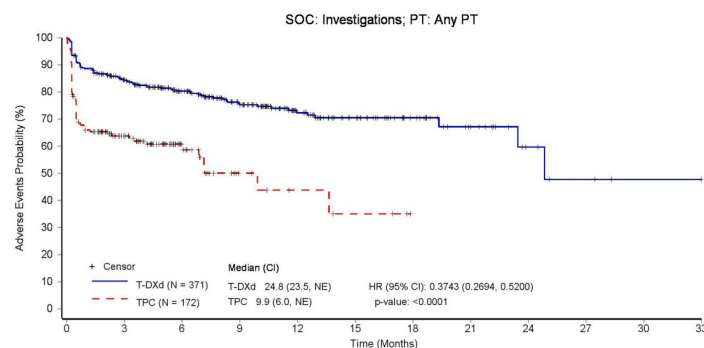
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DE.F.4.11.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT)  
 with incidence >= 5% in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	275	203	145	85	55	31	15	6	3	1	0
TPC (N = 172)	172	70	28	9	5	3	0	0	0	0	0	0

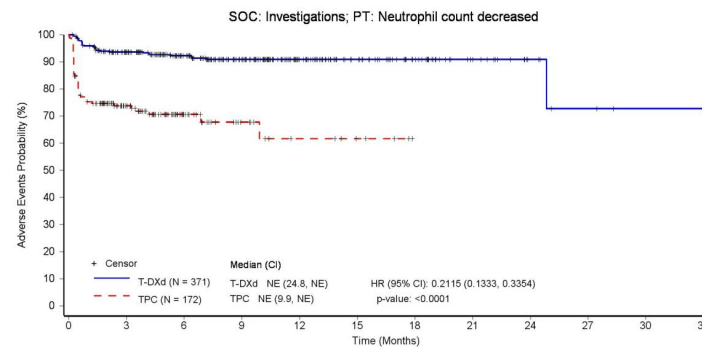
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

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DE.F.4.11.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT)  
 with incidence >= 5% in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	295	222	162	99	65	39	17	7	3	1	0
TPC (N = 172)	172	78	31	14	7	4	0	0	0	0	0	0

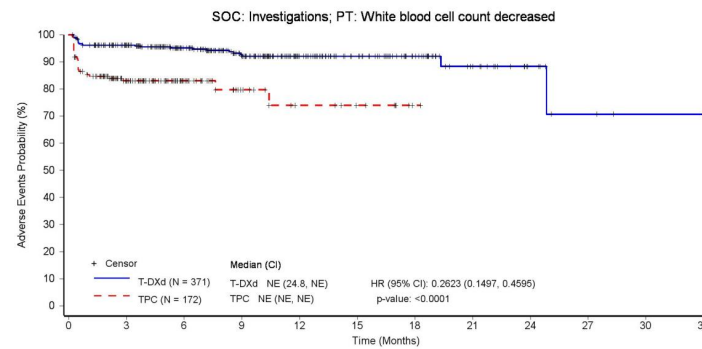
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

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DE.F.4.11.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT)  
 with incidence >= 5% in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	303	227	165	102	69	41	19	8	3	1	0
TPC (N = 172)	172	89	40	18	10	7	1	0	0	0	0	0

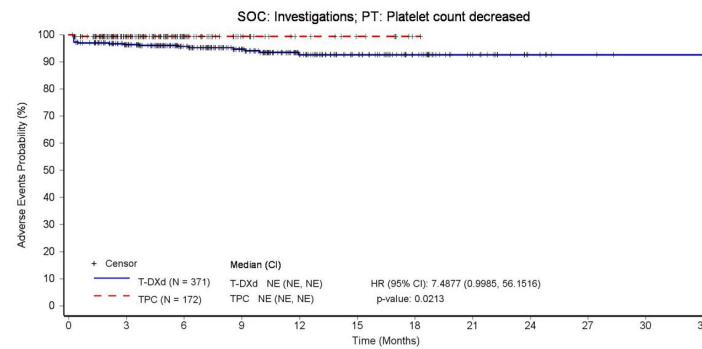
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

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DE.F.4.11.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	303	229	169	106	70	41	19	7	3	1	0
TPC (N = 172)	172	106	44	20	11	7	1	0	0	0	0	0

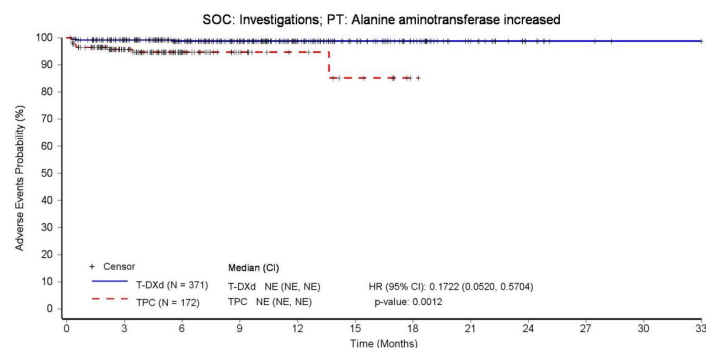
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

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DE.F.4.11.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT)  
 with incidence >= 5% in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	311	235	174	110	72	43	20	8	3	1	0
TPC (N = 172)	172	103	42	18	11	7	1	0	0	0	0	0

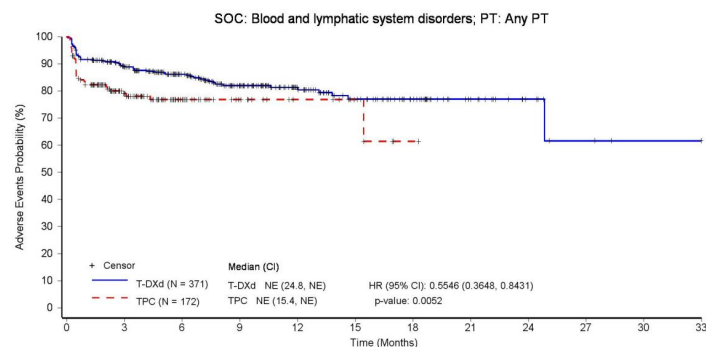
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

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DE.F.4.11.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT)  
 with incidence >= 5% in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	282	207	145	91	59	38	18	8	3	1	0
TPC (N = 172)	172	83	34	16	8	5	1	0	0	0	0	0

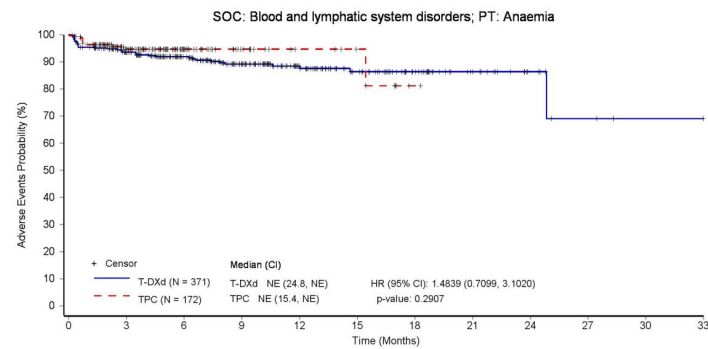
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DE.F.4.11.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT)  
 with incidence >= 5% in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	296	222	159	102	68	41	19	8	3	1	0
TPC (N = 172)	172	102	42	19	10	7	1	0	0	0	0	0

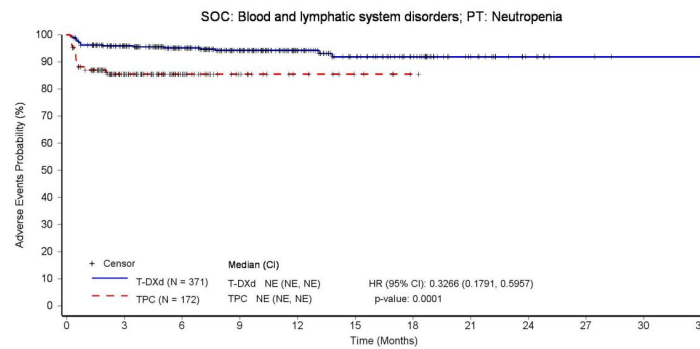
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DE.F.4.11.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT)  
 with incidence >= 5% in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	300	223	160	99	63	41	19	8	3	1	0
TPC (N = 172)	172	89	38	17	9	5	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

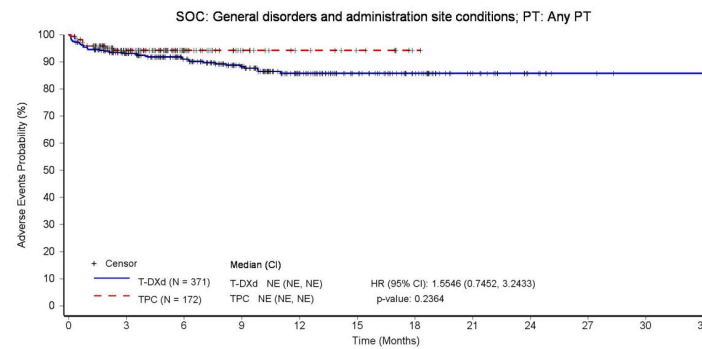
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DE.F.4.11.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT)  
 with incidence >= 5% in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

T-DXd (N = 371)	371	295	224	166	106	70	43	20	8	3	1	0
TPC (N = 172)	172	100	42	19	11	7	1	0	0	0	0	0

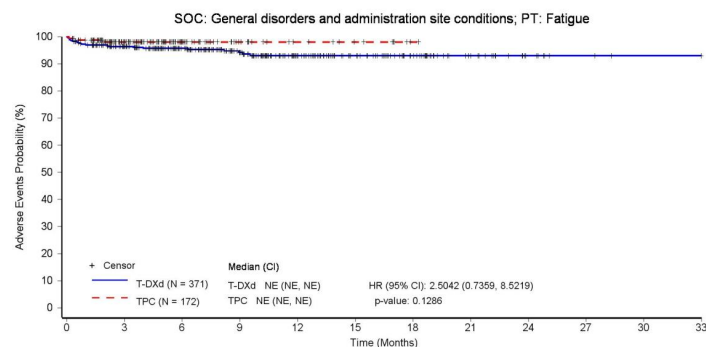
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DE.F.4.11.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	303	232	169	108	71	43	20	8	3	1	0
TPC (N = 172)	172	104	44	20	11	7	1	0	0	0	0	0

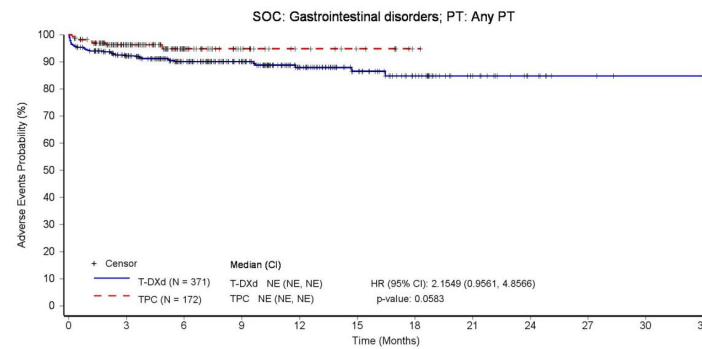
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

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DE.F.4.11.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) with incidence  $\geq 5\%$  in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	289	217	158	96	61	39	18	8	3	1	0
TPC (N = 172)	172	105	42	20	11	7	1	0	0	0	0	0

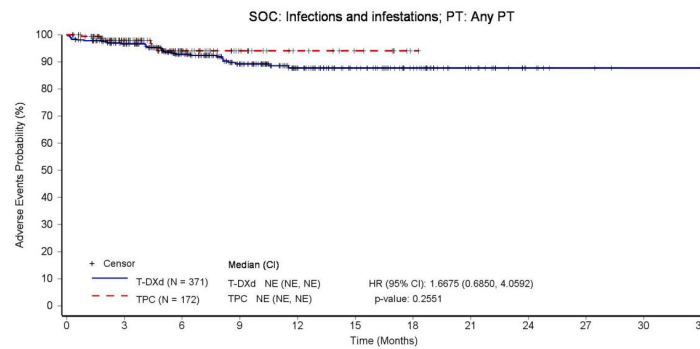
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DE.F.4.11.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT)  
 with incidence >= 5% in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	310	229	162	99	66	41	19	7	3	1	0
TPC (N = 172)	172	105	42	20	11	7	1	0	0	0	0	0

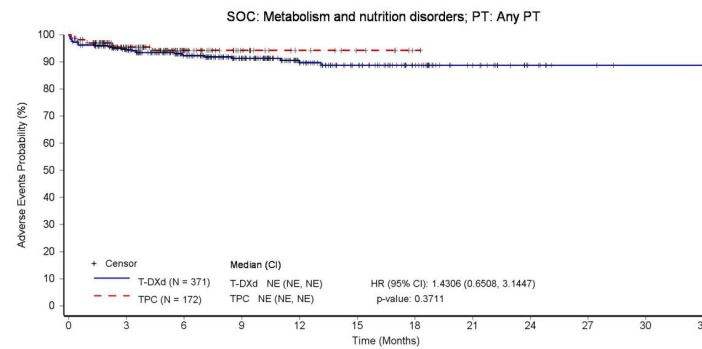
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Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.11.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	301	225	166	102	68	40	20	8	3	1	0
TPC (N = 172)	172	104	42	19	10	6	1	0	0	0	0	0

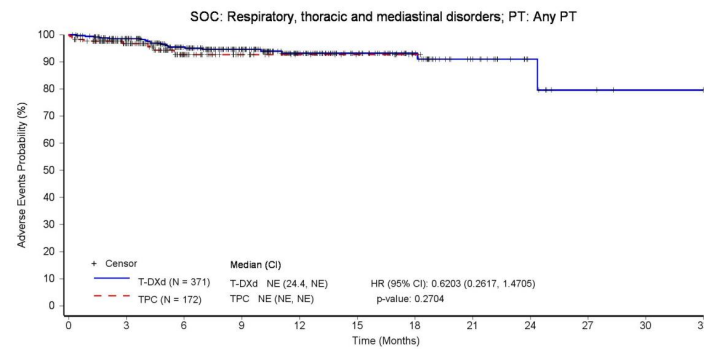
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Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.11.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT)  
 with incidence >= 5% in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	312	235	171	107	71	43	20	8	3	1	0
TPC (N = 172)	172	104	43	19	10	6	1	0	0	0	0	0

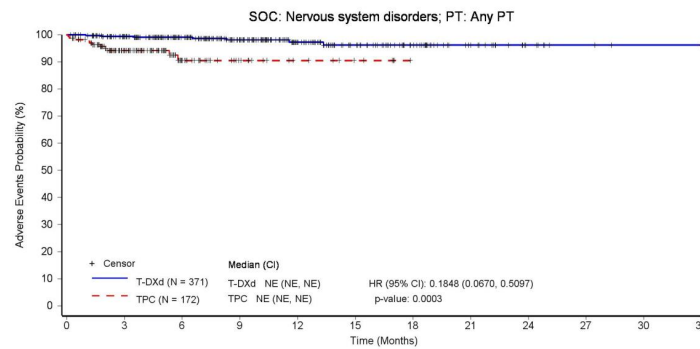
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DE.F.4.11.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT)  
 with incidence >= 5% in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	313	236	171	107	71	43	20	8	3	1	0
TPC (N = 172)	172	101	38	17	9	5	0	0	0	0	0	0

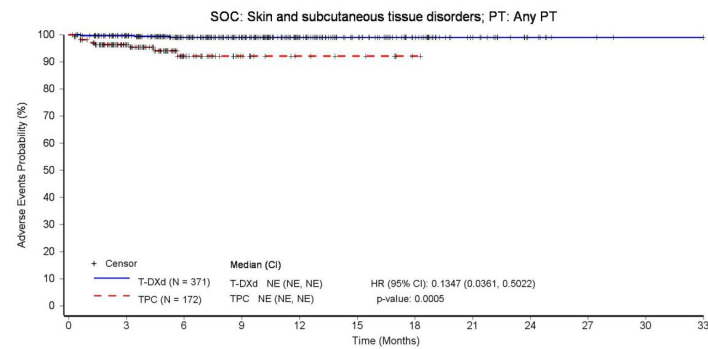
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.11.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - full analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	313	237	174	110	73	44	20	8	3	1	0
TPC (N = 172)	172	104	38	16	8	6	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

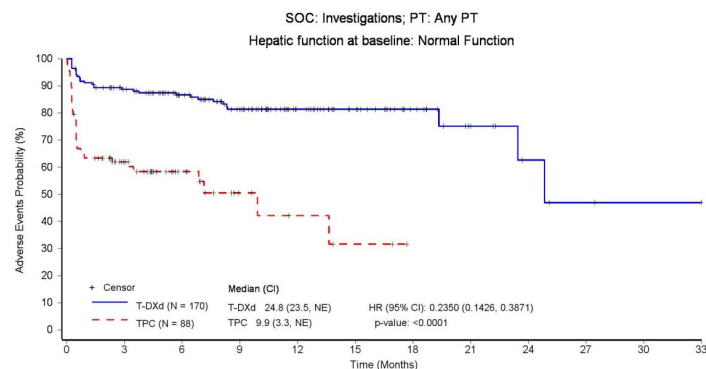
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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 170)	170	139	111	85	51	34	18	8	4	2	1	0
TPC (N = 88)	88	37	18	7	4	2	0	0	0	0	0	0

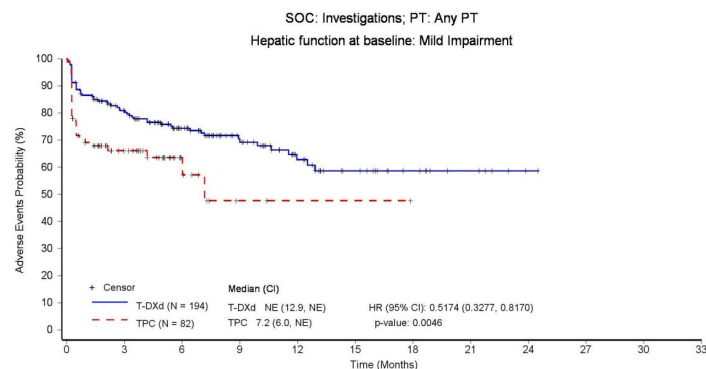
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 194)	194	133	90	58	33	20	12	6	1	0	0	0
TPC (N = 82)	82	33	10	2	1	1	0	0	0	0	0	0

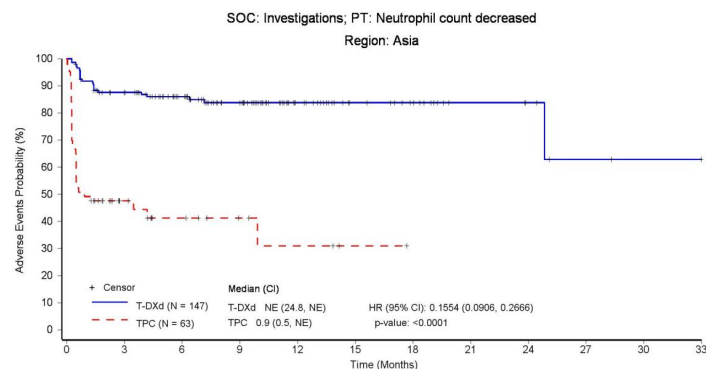
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) with incidence  $\geq 5\%$  in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

T-DXd (N = 147)	147	115	86	65	33	20	15	7	5	2	1	0
TPC (N = 63)	63	63	16	9	5	3	1	0	0	0	0	0

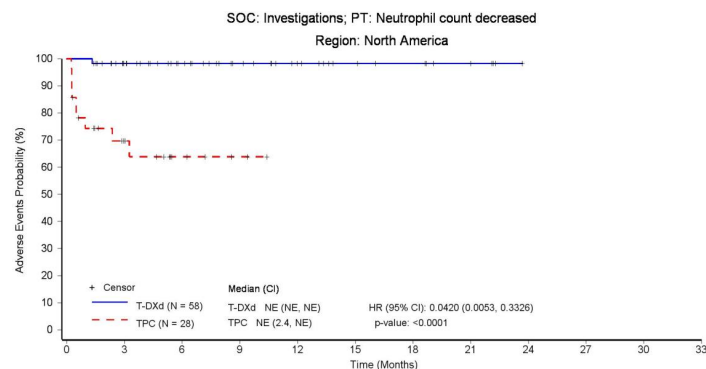
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) with incidence  $\geq 5\%$  in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 58)	58	45	34	25	17	11	8	4	0	0	0	0
TPC (N = 28)	28	13	5	2	0	0	0	0	0	0	0	0

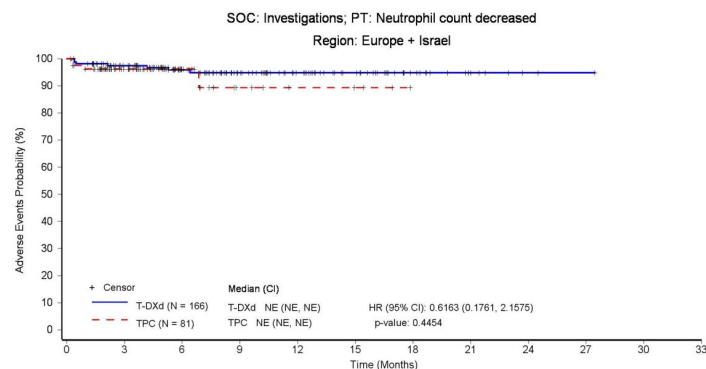
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 166)	166	135	102	72	49	34	16	6	2	1	0	0
TPC (N = 81)	81	49	17	7	4	3	0	0	0	0	0	0

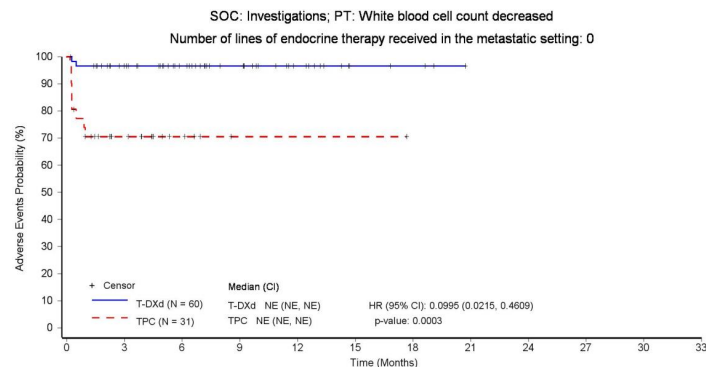
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 60)	60	47	32	22	12	4	3	0	0	0	0	0
TPC (N = 31)	31	13	5	1	1	1	0	0	0	0	0	0

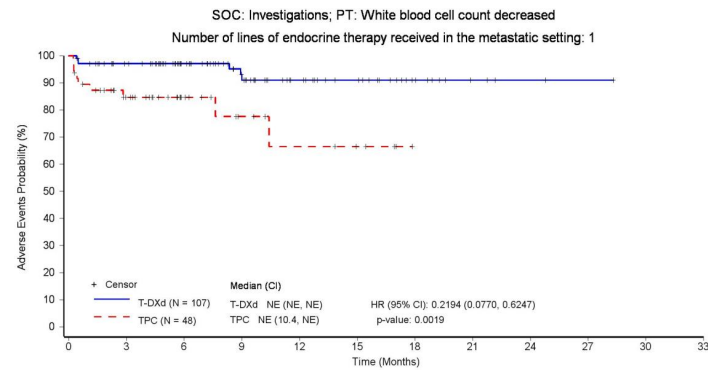
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 107)	107	89	65	44	28	20	10	4	2	1	0	0
TPC (N = 48)	48	30	16	9	6	4	0	0	0	0	0	0

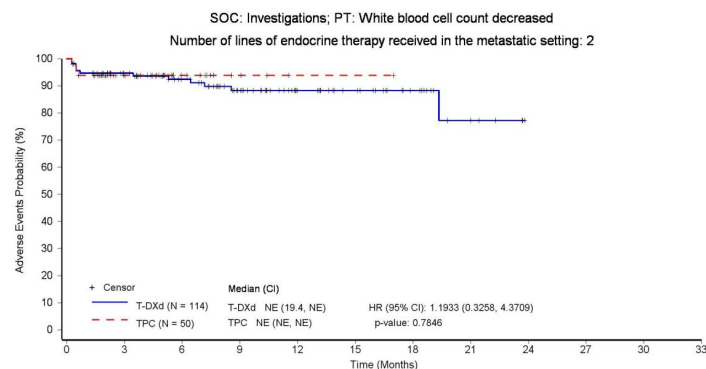
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 114)	114	89	73	55	35	25	14	5	0	0	0	0
TPC (N = 50)	50	27	11	4	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

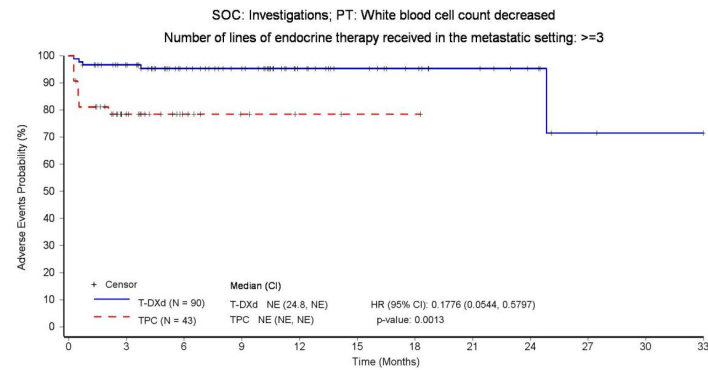
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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 90)	90	78	57	44	27	20	14	10	6	2	1	0
TPC (N = 43)	43	19	8	4	2	1	1	0	0	0	0	0

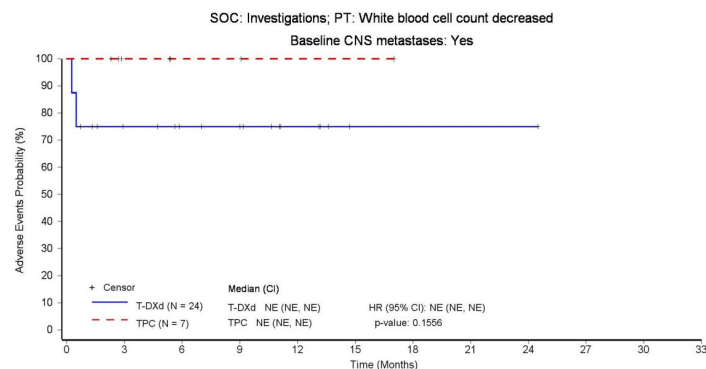
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 24)	24	14	11	10	5	1	1	1	1	0	0	0
TPC (N = 7)	7	4	2	2	1	1	0	0	0	0	0	0

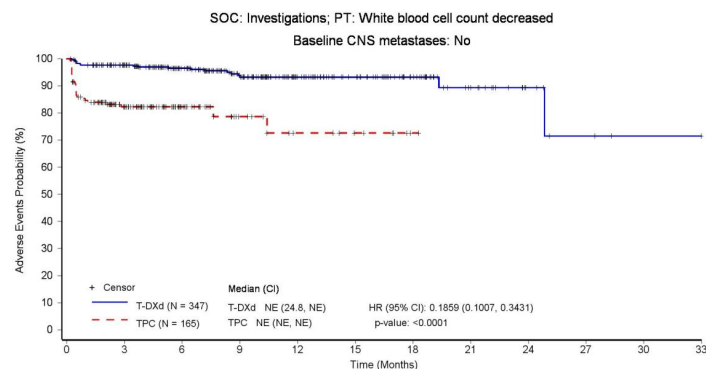
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 347)	347	289	216	155	97	68	40	18	7	3	1	0
TPC (N = 165)	165	85	38	16	9	6	1	0	0	0	0	0

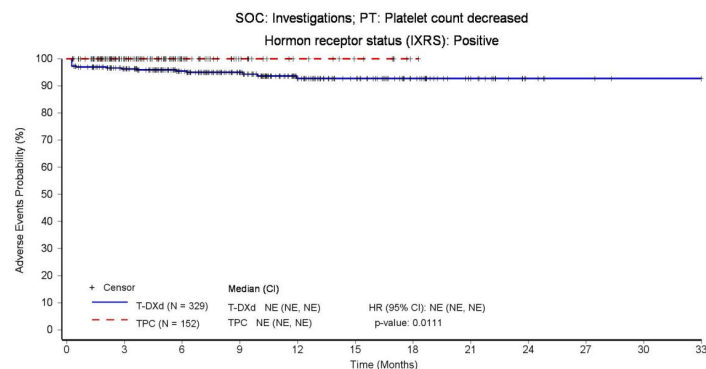
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

T-DXd (N = 329)	329	273	209	156	98	65	37	18	6	3	1	0
TPC (N = 152)	152	95	41	20	11	7	1	0	0	0	0	0

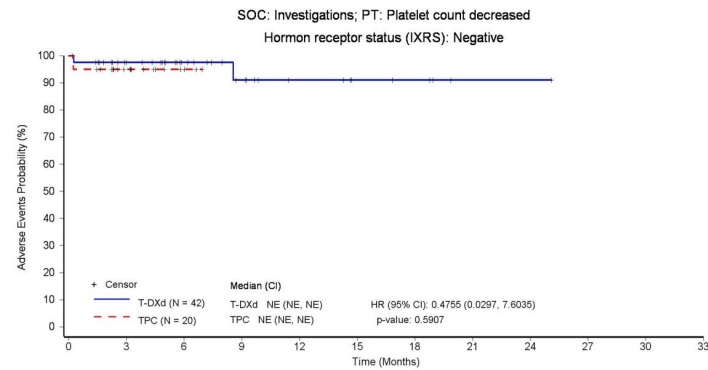
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 42)	42	30	20	13	8	5	4	1	1	0	0	0
TPC (N = 20)	20	11	3	0	0	0	0	0	0	0	0	0

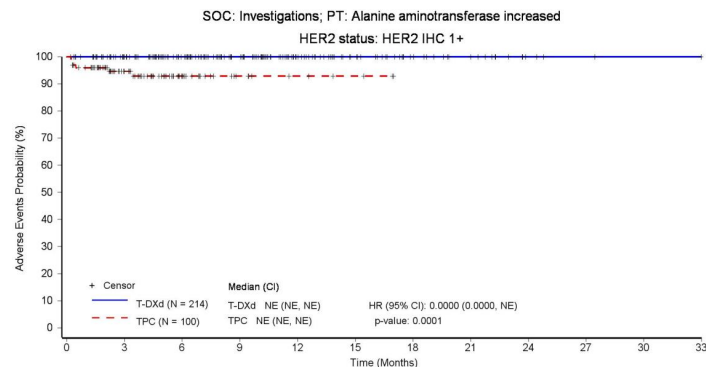
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 214)	214	178	138	101	62	39	23	13	4	2	1	0
TPC (N = 100)	100	58	25	9	5	3	0	0	0	0	0	0

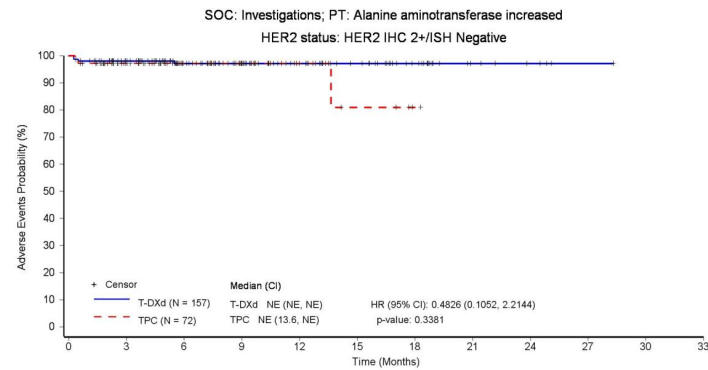
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 157)	157	133	97	73	48	33	20	7	4	1	0	0
TPC (N = 72)	72	45	17	9	6	4	1	0	0	0	0	0

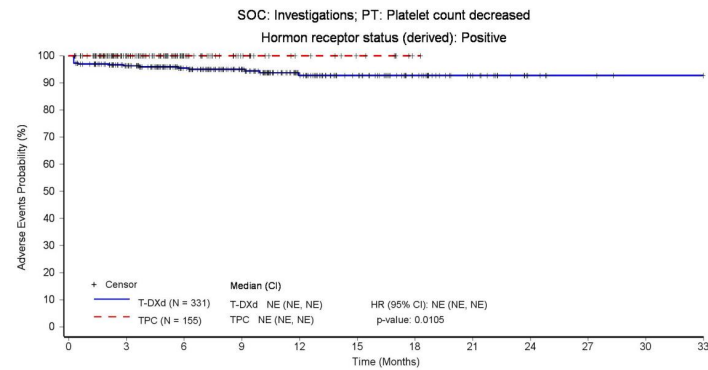
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 331)	331	274	209	157	99	66	38	18	6	3	1	0
TPC (N = 155)	155	98	41	20	11	7	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

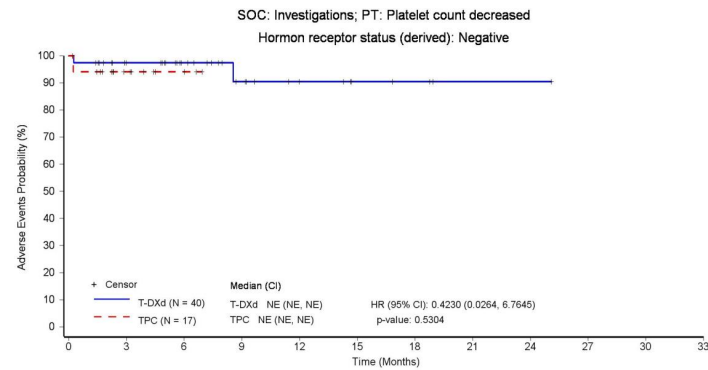
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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 40)	40	29	20	12	7	4	3	1	1	0	0	0
TPC (N = 17)	17	8	3	0	0	0	0	0	0	0	0	0

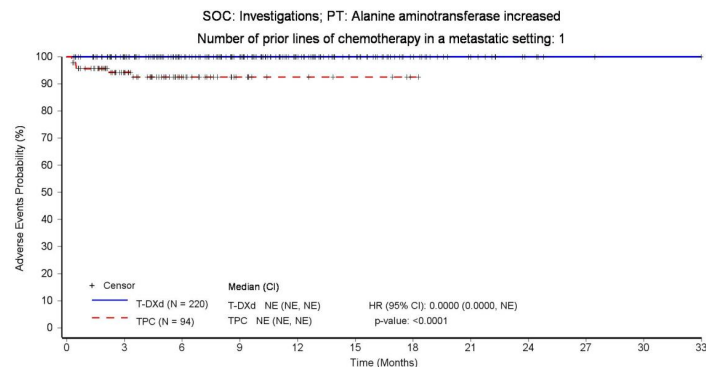
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) with incidence  $\geq 5\%$  in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 220)	220	186	139	108	69	45	23	12	5	2	1	0
TPC (N = 94)	94	57	26	11	6	4	1	0	0	0	0	0

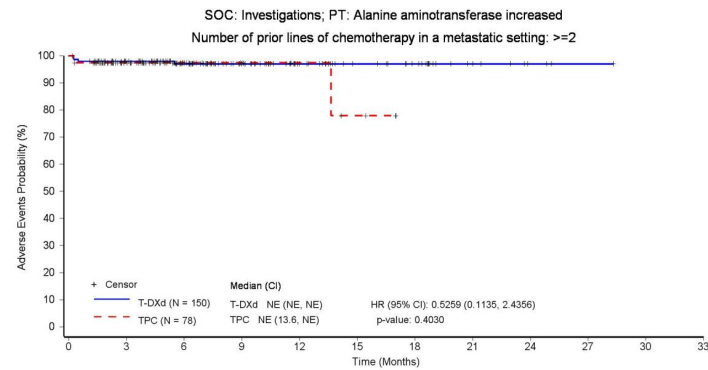
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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 Run date: 21OCT2022 – 17:57; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESEVSOCPT5PER\_4\_SAS.rtf

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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 150)	150	124	95	65	40	26	19	7	3	1	0	0
TPC (N = 78)	78	46	16	7	5	3	0	0	0	0	0	0

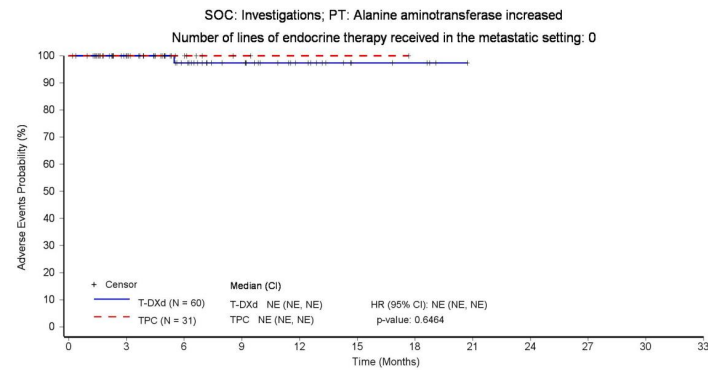
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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 Run date: 21OCT2022 – 17:57; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESEVSOCPT5PER\_4\_SAS.rtf

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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

T-DXd (N = 60)	60	49	33	23	13	5	4	0	0	0	0	0
TPC (N = 31)	31	18	7	2	1	1	0	0	0	0	0	0

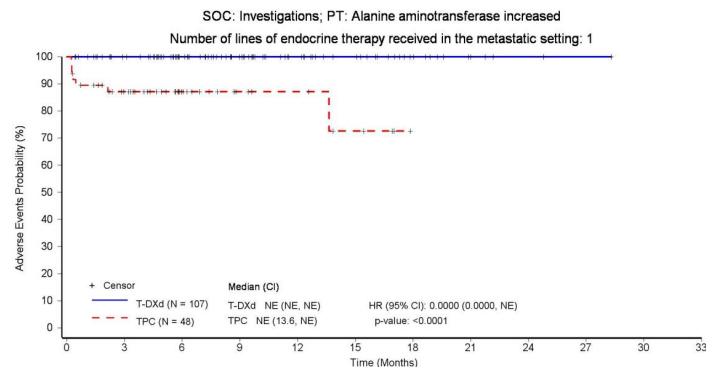
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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 Run date: 21OCT2022 – 17:57; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESEVSOCPT5PER\_4\_SAS.rtf

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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 107)	107	91	67	47	31	22	11	4	2	1	0	0
TPC (N = 48)	48	33	17	9	7	4	0	0	0	0	0	0

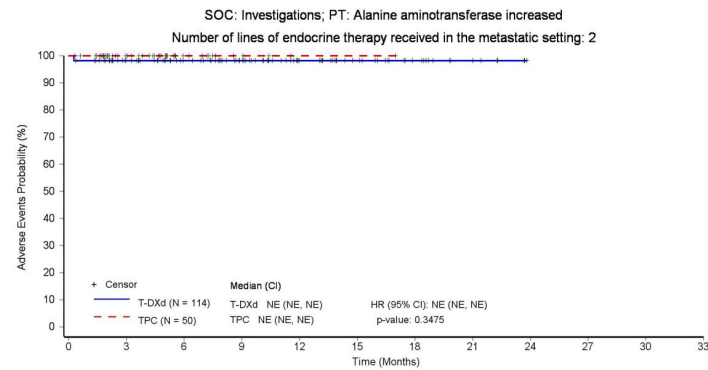
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

T-DXd (N = 114)	114	91	75	59	38	25	14	6	0	0	0	0
TPC (N = 50)	50	30	11	4	1	1	0	0	0	0	0	0

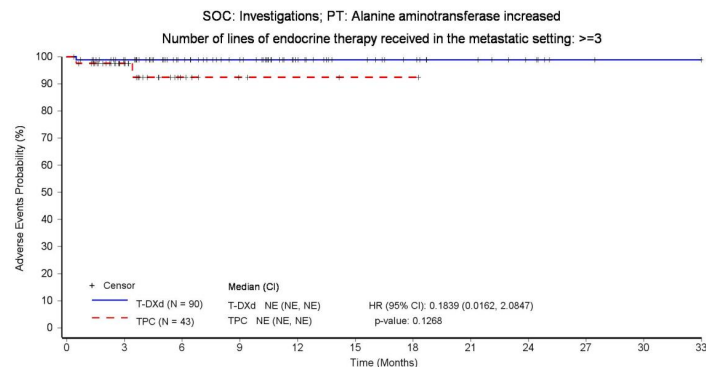
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 90)	90	80	60	45	28	20	14	10	6	2	1	0
TPC (N = 43)	43	22	7	3	2	1	1	0	0	0	0	0

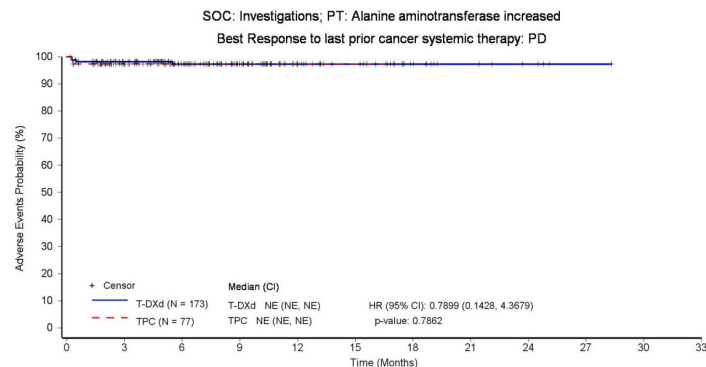
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) with incidence  $\geq 5\%$  in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 173)	173	141	100	70	39	27	14	7	4	1	0	0
TPC (N = 77)	77	44	18	6	2	2	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

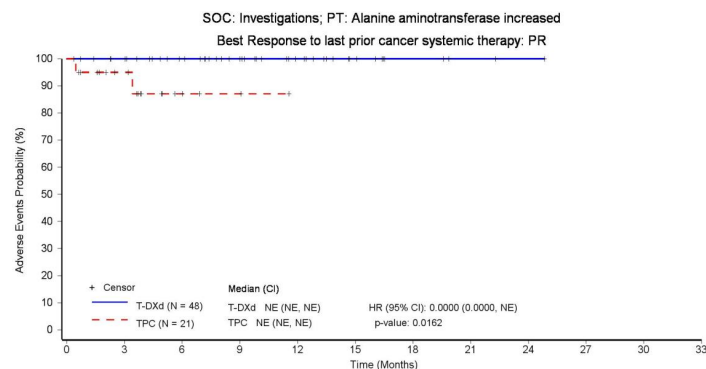
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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 48)	48	44	36	27	17	9	4	2	1	0	0	0
TPC (N = 21)	21	13	4	2	0	0	0	0	0	0	0	0

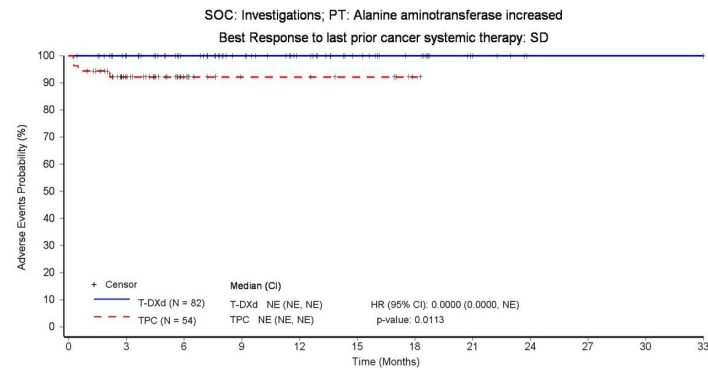
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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 Run date: 21OCT2022 – 17:57; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESEVSOCPT5PER\_4\_SAS.rtf

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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 82)	82	67	53	41	31	21	15	5	1	1	1	0
TPC (N = 54)	54	33	15	7	7	5	1	0	0	0	0	0

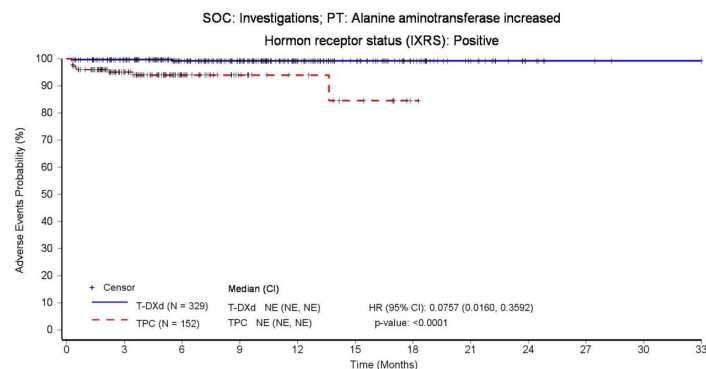
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 329)	329	282	216	161	102	67	39	19	7	3	1	0
TPC (N = 152)	152	91	39	18	11	7	1	0	0	0	0	0

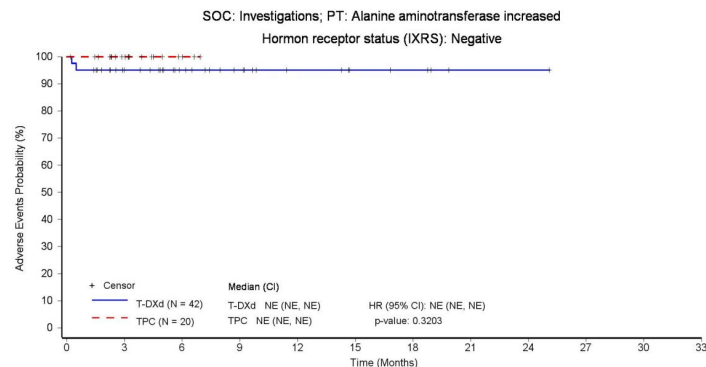
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

T-DXd (N = 42)	42	29	19	13	8	5	4	1	1	0	0	0
TPC (N = 20)	20	12	3	0	0	0	0	0	0	0	0	0

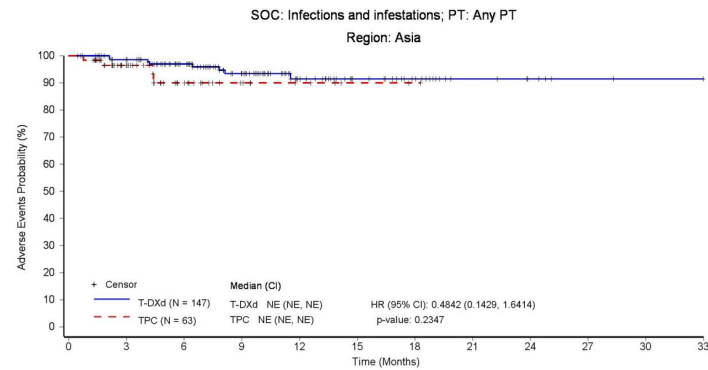
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

T-DXd (N = 147)	147	131	99	71	39	25	17	8	5	2	1	0
TPC (N = 63)	63	39	19	9	5	2	1	0	0	0	0	0

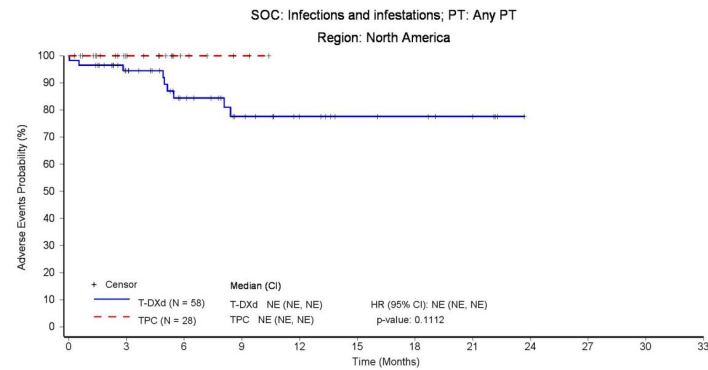
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Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 58)	58	44	30	21	14	9	7	4	0	0	0	0
TPC (N = 28)	28	15	5	2	0	0	0	0	0	0	0	0

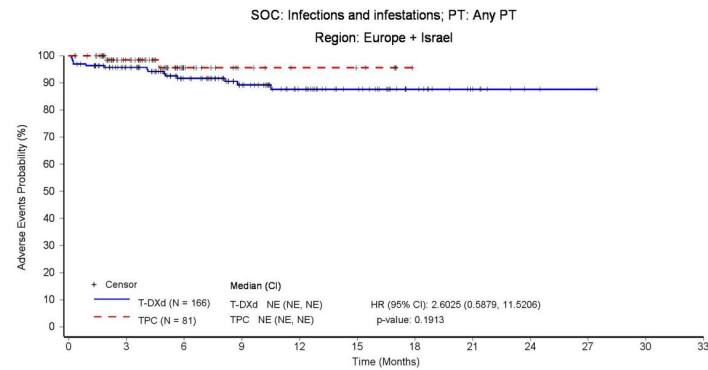
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 166)	166	135	100	70	46	32	17	7	2	1	0	0
TPC (N = 81)	81	51	18	9	6	5	0	0	0	0	0	0

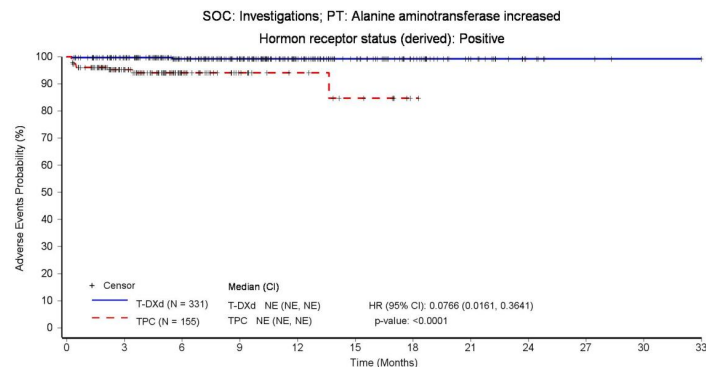
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 331)	331	283	216	162	103	68	40	19	7	3	1	0
TPC (N = 155)	155	94	39	18	11	7	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

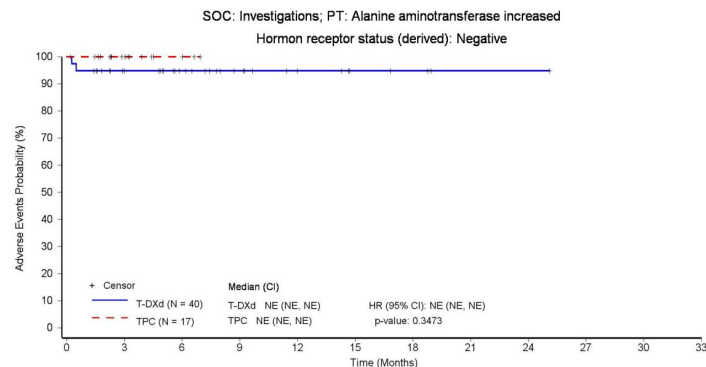
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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

T-DXd (N = 40)	40	28	19	12	7	4	3	1	1	0	0	0
TPC (N = 17)	17	9	3	0	0	0	0	0	0	0	0	0

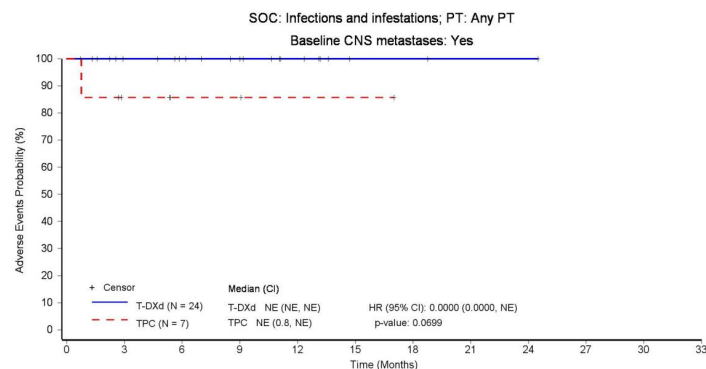
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 24)	24	18	15	12	7	2	2	1	1	0	0	0
TPC (N = 7)	7	4	2	2	1	1	0	0	0	0	0	0

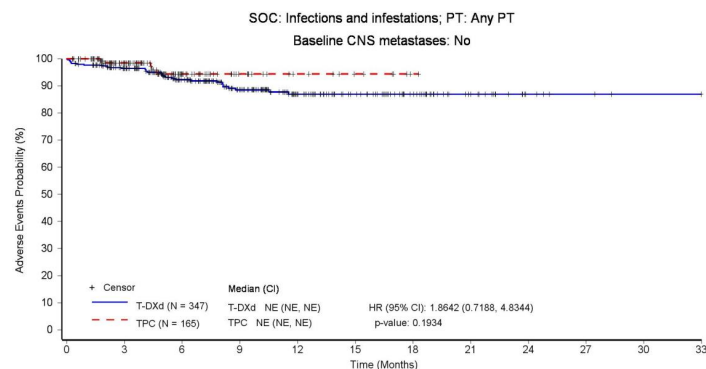
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:57; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESEVSOCPT5PER\_4\_SAS.rtf

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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 347)	347	292	214	150	92	64	39	18	6	3	1	0
TPC (N = 165)	165	101	40	18	10	6	1	0	0	0	0	0

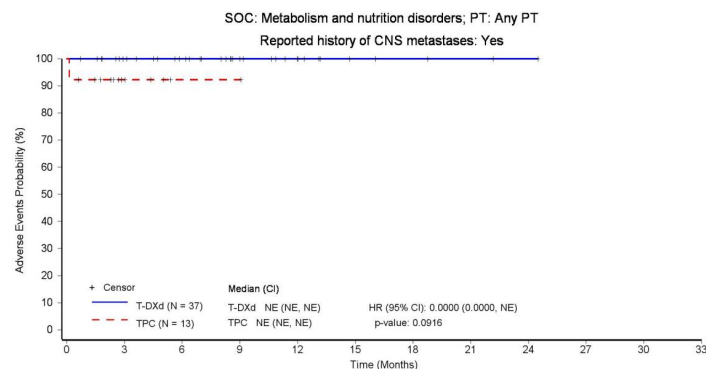
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:57; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESEVSOCPT5PER\_4\_SAS.rtf

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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 37)	37	30	24	15	9	4	3	2	1	0	0	0
TPC (N = 13)	13	5	1	1	0	0	0	0	0	0	0	0

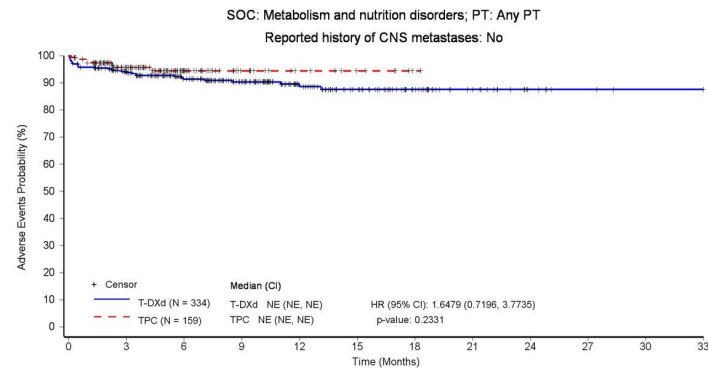
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:57; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESEVSOCPT5PER\_4\_SAS.rtf

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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 334)	334	271	201	151	93	64	37	18	7	3	1	0
TPC (N = 159)	159	99	41	18	10	6	1	0	0	0	0	0

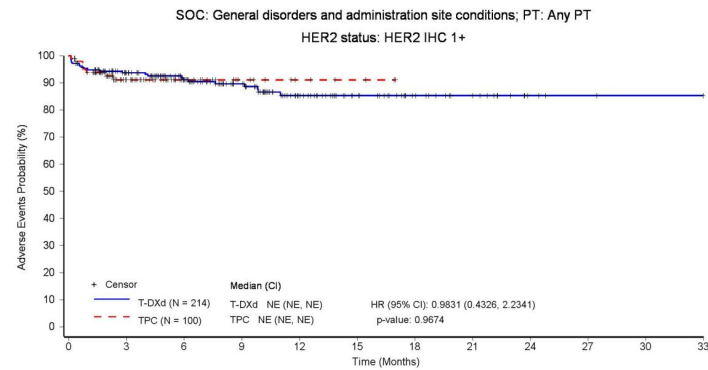
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

T-DXd (N = 214)	214	167	128	97	59	38	23	13	4	2	1	0
TPC (N = 100)	100	54	25	10	5	3	0	0	0	0	0	0

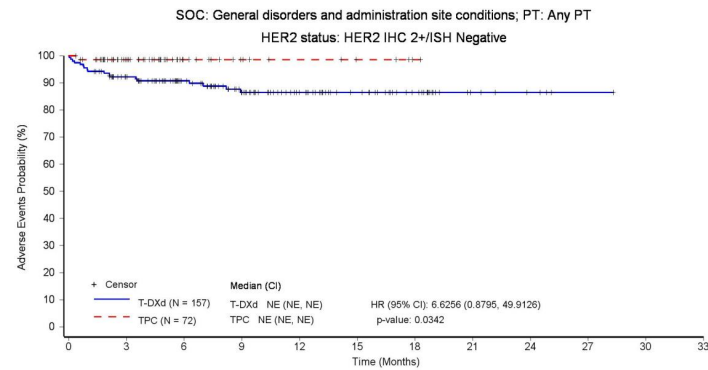
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 157)	157	128	96	69	47	32	20	7	4	1	0	0
TPC (N = 72)	72	46	17	9	6	4	1	0	0	0	0	0

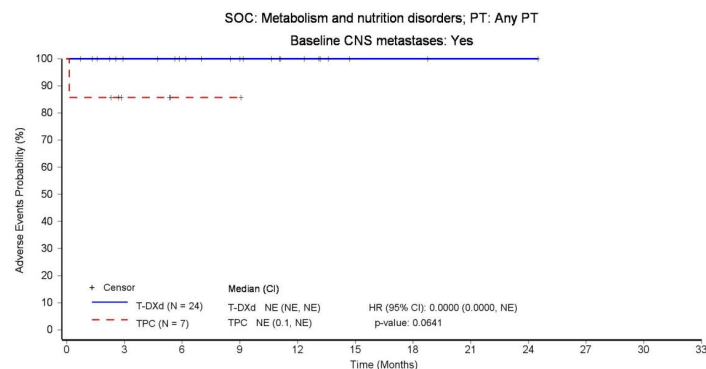
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 24)	24	18	15	12	7	2	2	1	1	0	0	0
TPC (N = 7)	7	3	1	1	0	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

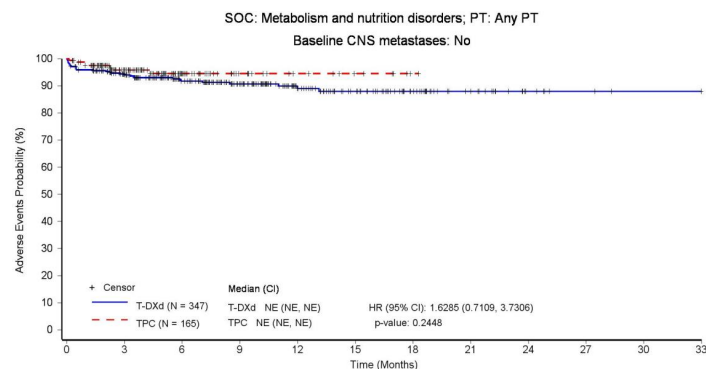
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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 347)	347	283	210	154	95	66	38	19	7	3	1	0
TPC (N = 165)	165	101	41	18	10	6	1	0	0	0	0	0

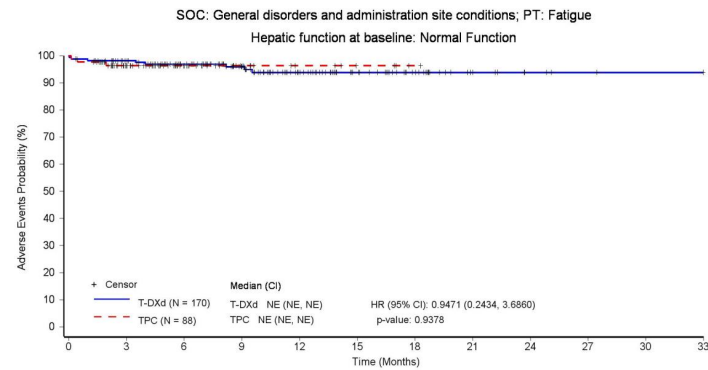
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 170)	170	152	124	96	61	39	22	8	4	2	1	0
TPC (N = 88)	88	58	28	13	7	4	1	0	0	0	0	0

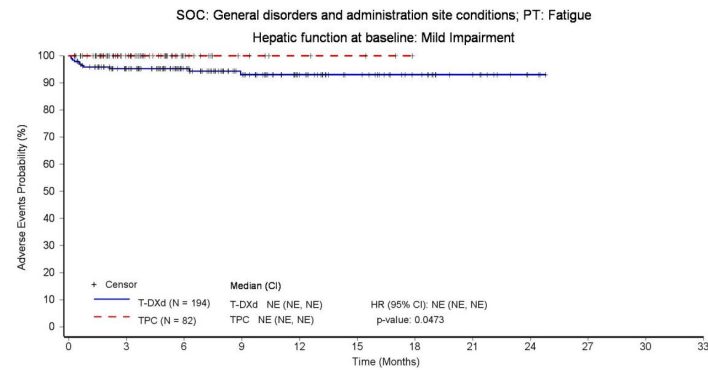
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 194)	194	149	106	71	46	31	20	11	3	0	0	0
TPC (N = 82)	82	46	16	7	4	3	0	0	0	0	0	0

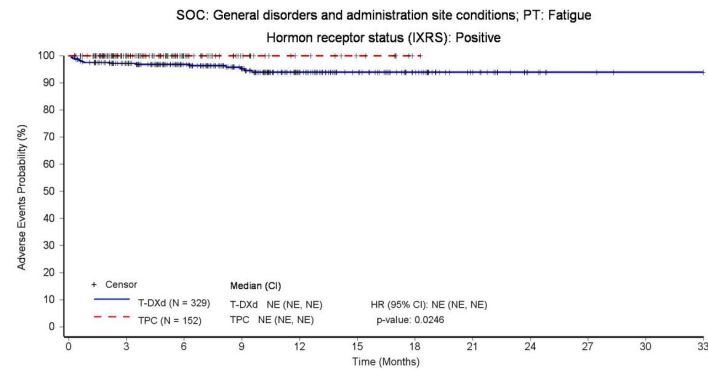
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 329)	329	275	213	157	100	66	39	19	7	3	1	0
TPC (N = 152)	152	95	41	20	11	7	1	0	0	0	0	0

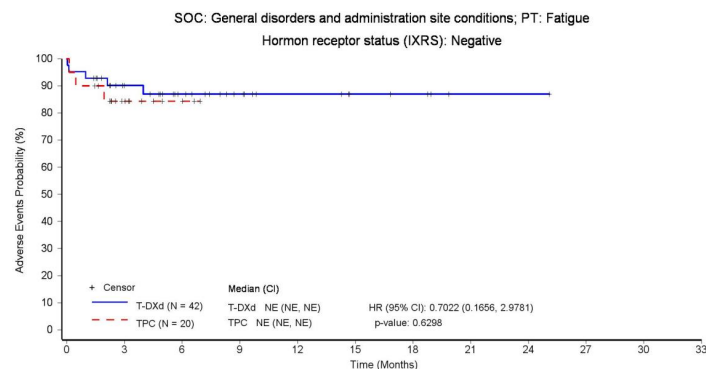
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 42)	42	28	19	12	8	5	4	1	1	0	0	0
TPC (N = 20)	20	9	3	0	0	0	0	0	0	0	0	0

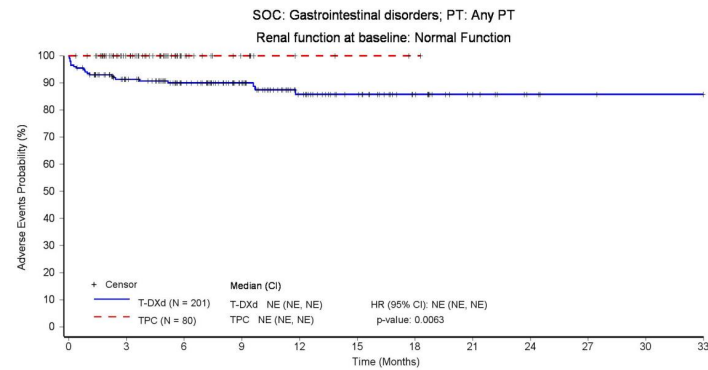
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) with incidence  $\geq 5\%$  in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 201)	201	156	114	83	49	34	20	9	4	2	1	0
TPC (N = 80)	80	49	18	8	3	2	1	0	0	0	0	0

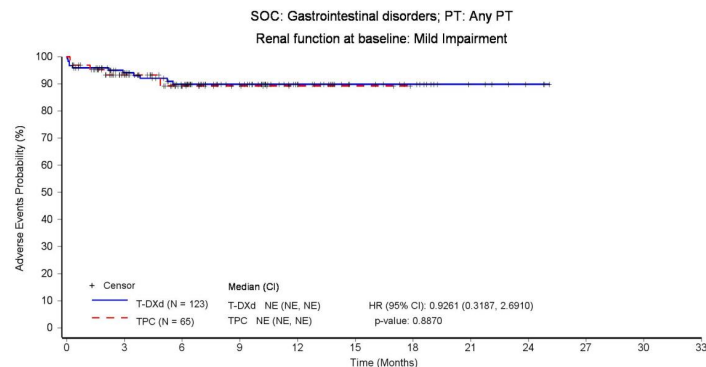
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 123)	123	98	75	54	33	19	15	7	3	0	0	0
TPC (N = 65)	65	36	13	6	2	2	0	0	0	0	0	0

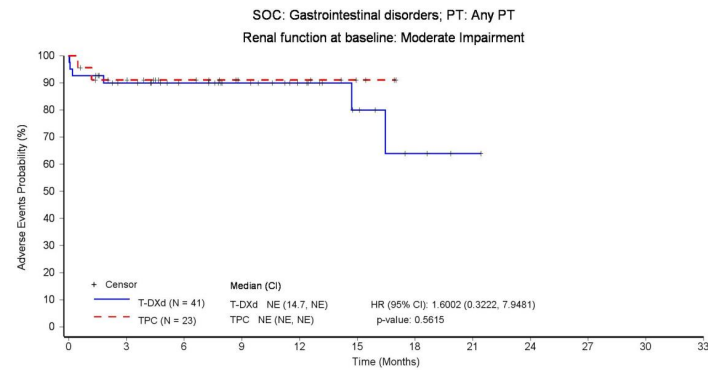
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 41)	41	31	25	19	13	7	3	1	0	0	0	0
TPC (N = 23)	23	18	11	6	6	3	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

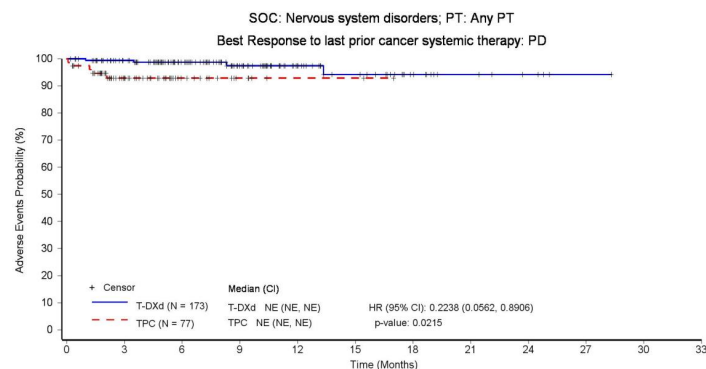
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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 173)	173	144	102	69	39	27	14	7	4	1	0	0
TPC (N = 77)	77	41	16	6	2	2	0	0	0	0	0	0

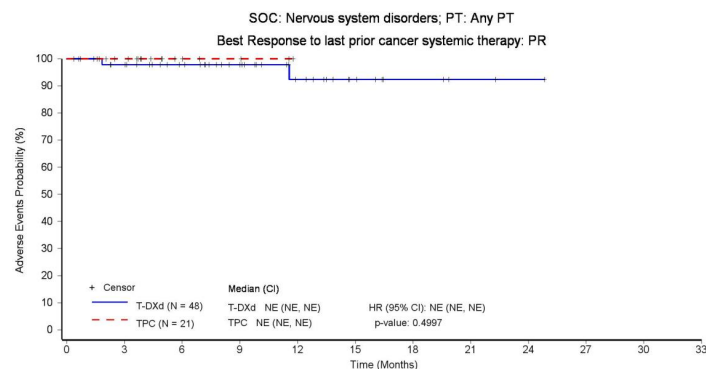
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 48)	48	43	35	26	15	8	4	2	1	0	0	0
TPC (N = 21)	21	14	5	3	0	0	0	0	0	0	0	0

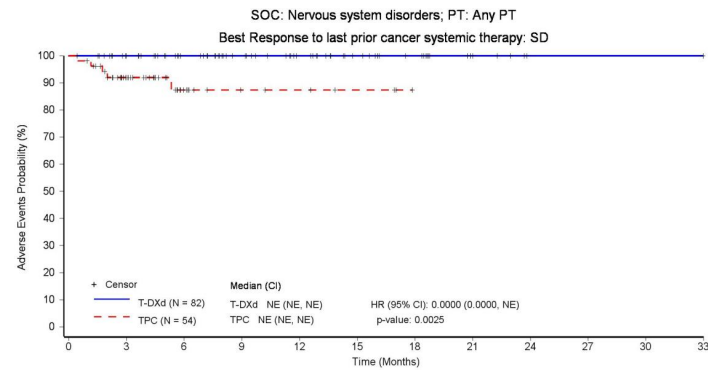
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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 82)	82	67	53	41	31	21	15	5	1	1	1	0
TPC (N = 54)	54	33	13	6	5	3	0	0	0	0	0	0

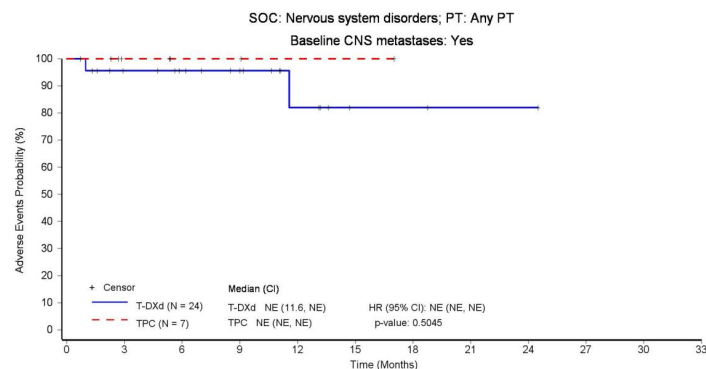
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:57; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESEVSOCPT5PER\_4\_SAS.rtf

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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 24)	24	18	15	12	6	2	2	1	1	0	0	0
TPC (N = 7)	7	4	2	2	1	1	0	0	0	0	0	0

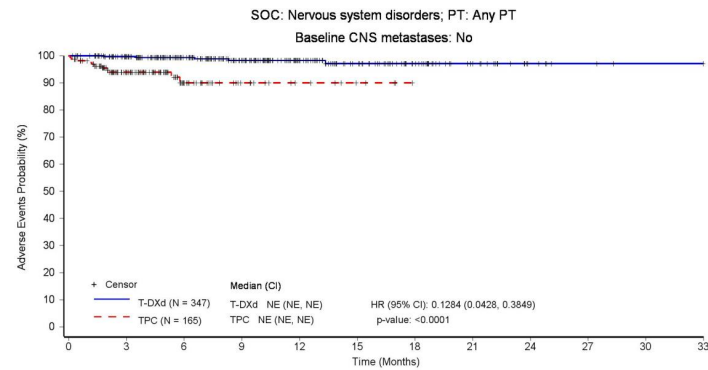
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:57; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESEVSOCPT5PER\_4\_SAS.rtf

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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) with incidence  $\geq 5\%$  in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 347)	347	295	221	159	101	69	41	19	7	3	1	0
TPC (N = 165)	165	97	36	15	8	4	0	0	0	0	0	0

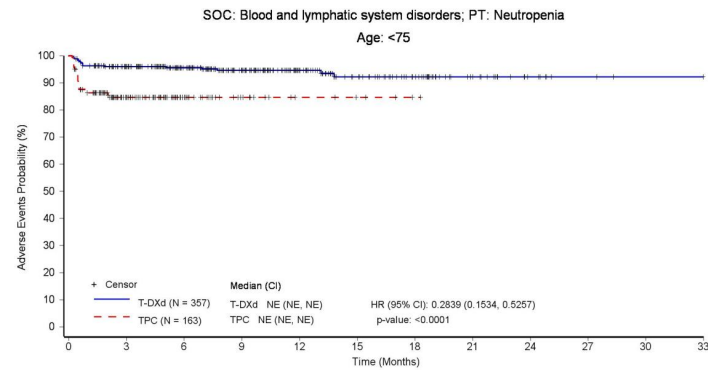
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:57; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESEVSOCPT5PER\_4\_SAS.rtf

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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) with incidence  $\geq 5\%$  in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 357)	357	289	215	156	97	62	41	19	8	3	1	0
TPC (N = 163)	163	81	33	14	6	4	1	0	0	0	0	0

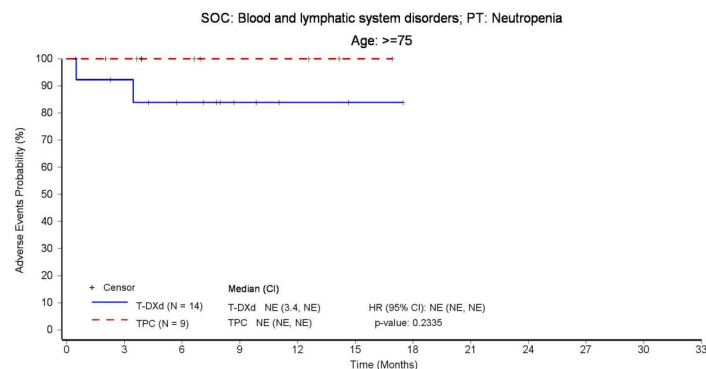
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:57; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESEVSOCPT5PER\_4\_SAS.rtf

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DE.F.4.11.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) with incidence >= 5% in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 14)	14	11	8	4	2	1	0	0	0	0	0	0
TPC (N = 9)	9	8	5	3	3	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 17:57; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESEVSOCPT5PER\_4\_SAS.rtf

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DE.T.4.12.1 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	89 (24.0)	70 (40.7)	
Number of subjects censored, n (%)	282 (76.0)	102 (59.3)	
Median time to first event (months) [a]	24.8	9.9	
95% Confidence Interval	[23.5, NE]	[6.0, NE]	
Stratified Cox proportional hazards model [b]			
Hazard Ratio			0.3743
95% Confidence Interval			[0.2694, 0.5200]
p-value			<0.0001
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 18:59; Program name: T4\_AESOCPT10PAT\_1\_SAS.sas; Output name: T4\_AESEVSOCPT10PAT\_1\_SAS.rtf



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DE.T.4.12.1 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Neutrophil count decreased

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	31 (8.4)	49 (28.5)	
Number of subjects censored, n (%)	340 (91.6)	123 (71.5)	
Median time to first event (months) [a] 95% Confidence Interval	NE [24.8, NE]	NE [9.9, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.2115 [0.1333, 0.3354] <0.0001
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
Run date: 13SEP2022 – 18:59; Program name: T4\_AESOCPT10PAT\_1\_SAS.sas; Output name: T4\_AESEVSOCPT10PAT\_1\_SAS.rtf

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DE.T.4.12.1 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: White blood cell count decreased

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	25 (6.7)	30 (17.4)	
Number of subjects censored, n (%)	346 (93.3)	142 (82.6)	
Median time to first event (months) [a] 95% Confidence Interval	NE [24.8, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.2623 [0.1497, 0.4595] <0.0001
Stratified log-rank p-value [c]			<0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 18:59; Program name: T4\_AESOCPT10PAT\_1\_SAS.sas; Output name: T4\_AESEVSOCPT10PAT\_1\_SAS.rtf

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DE.T.4.12.1 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Platelet count decreased

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	20 (5.4)	1 (0.6)	
Number of subjects censored, n (%)	351 (94.6)	171 (99.4)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			7.4877 [0.9985, 56.1516] 0.0502
Stratified log-rank p-value [c]			0.0213

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 18:59; Program name: T4\_AESOCPT10PAT\_1\_SAS.sas; Output name: T4\_AESEVSOCPT10PAT\_1\_SAS.rtf

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DE.T.4.12.1 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Lymphocyte count decreased

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	18 (4.9)	5 (2.9)	
Number of subjects censored, n (%)	353 (95.1)	167 (97.1)	
Median time to first event (months) [a] 95% Confidence Interval	NE [24.8, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.9802 [0.3493, 2.7511] 0.9698
Stratified log-rank p-value [c]			0.9699

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
Run date: 13SEP2022 – 18:59; Program name: T4\_AESOCPT10PAT\_1\_SAS.sas; Output name: T4\_AESEVSOCPT10PAT\_1\_SAS.rtf

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DE.T.4.12.1 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Aspartate aminotransferase increased

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	12 (3.2)	8 (4.7)	
Number of subjects censored, n (%)	359 (96.8)	164 (95.3)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.6136 [0.2485, 1.5156] 0.2898
Stratified log-rank p-value [c]			0.2852

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.12.1 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	63 (17.0)	37 (21.5)	
Number of subjects censored, n (%)	308 (83.0)	135 (78.5)	
Median time to first event (months) [a] 95% Confidence Interval	NE [24.8, NE]	NE [15.4, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.5546 [0.3648, 0.8431] 0.0058
Stratified log-rank p-value [c]			0.0052

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.12.1 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Anaemia

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	38 (10.2)	9 (5.2)	
Number of subjects censored, n (%)	333 (89.8)	163 (94.8)	
Median time to first event (months) [a] 95% Confidence Interval	NE [24.8, NE]	NE [15.4, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.4839 [0.7099, 3.1020] 0.2941
Stratified log-rank p-value [c]			0.2907

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.12.1 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Neutropenia

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	21 (5.7)	24 (14.0)	
Number of subjects censored, n (%)	350 (94.3)	148 (86.0)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.3266 [0.1791, 0.5957] 0.0003
Stratified log-rank p-value [c]			0.0001

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.12.1 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: General disorders and administration site conditions; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	41 (11.1)	9 (5.2)	
Number of subjects censored, n (%)	330 (88.9)	163 (94.8)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.5546 [0.7452, 3.2433] 0.2396
Stratified log-rank p-value [c]			0.2364

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: General disorders and administration site conditions; PT: Fatigue

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	20 (5.4)	3 (1.7)	
Number of subjects censored, n (%)	351 (94.6)	169 (98.3)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			2.5042 [0.7359, 8.5219] 0.1418
Stratified log-rank p-value [c]			0.1286

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Gastrointestinal disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	39 (10.5)	7 (4.1)	
Number of subjects censored, n (%)	332 (89.5)	165 (95.9)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			2.1549 [0.9561, 4.8566] 0.0641
Stratified log-rank p-value [c]			0.0583

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Gastrointestinal disorders; PT: Nausea

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	17 (4.6)	0	
Number of subjects censored, n (%)	354 (95.4)	172 (100)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			NE [0.0000, NE] 0.9912
Stratified log-rank p-value [c]			0.0074

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors.

Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Infections and infestations; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	32 (8.6)	6 (3.5)	
Number of subjects censored, n (%)	339 (91.4)	166 (96.5)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.6675 [0.6850, 4.0592] 0.2599
Stratified log-rank p-value [c]			0.2551

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Metabolism and nutrition disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	31 (8.4)	8 (4.7)	
Number of subjects censored, n (%)	340 (91.6)	164 (95.3)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.4306 [0.6508, 3.1447] 0.3729
Stratified log-rank p-value [c]			0.3711

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	10 (2.7)	2 (1.2)	
Number of subjects censored, n (%)	361 (97.3)	170 (98.8)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			1.7857 [0.3838, 8.3087] 0.4598
Stratified log-rank p-value [c]			0.4545

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	20 (5.4)	8 (4.7)	
Number of subjects censored, n (%)	351 (94.6)	164 (95.3)	
Median time to first event (months) [a] 95% Confidence Interval	NE [24.4, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.6203 [0.2617, 1.4705] 0.2782
Stratified log-rank p-value [c]			0.2704

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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SOC: Nervous system disorders; PT: Any PT

	T-DXd (N=371)	TPC (N=172)	Analysis T-DXd vs TPC
Number of subjects with events, n (%)	7 (1.9)	11 (6.4)	
Number of subjects censored, n (%)	364 (98.1)	161 (93.6)	
Median time to first event (months) [a] 95% Confidence Interval	NE [NE, NE]	NE [NE, NE]	
Stratified Cox proportional hazards model [b] Hazard Ratio 95% Confidence Interval p-value			0.1848 [0.0670, 0.5097] 0.0011
Stratified log-rank p-value [c]			0.0003

N: number of subjects in analysis set; %: proportion of number of subjects in analysis set; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model with treatment as the only categorical variable in the model, stratified by the randomization stratification factors. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors.

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DE.T.4.12.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.5117
HER2 IHC 1+	214	50 (23.4)	164 (76.6)	NE (23.5, NE)	100	41 (41.0)	59 (59.0)	NE (2.4, NE)	0.3281 (0.2129, 0.5055) <0.0001	<0.0001	
HER2 IHC 2+/ISH Negative	157	39 (24.8)	118 (75.2)	24.8 (24.8, NE)	72	29 (40.3)	43 (59.7)	7.1 (6.0, NE)	0.4244 (0.2585, 0.6968) 0.0007	0.0005	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	No. of subjects Nsub with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting									0.4185
1	220	45 (20.5)	175 (79.5) NE (23.5, NE)	94	30 (31.9)	64 (68.1) NE (6.9, NE)	0.4360 (0.2715, 0.7001) 0.0006	0.0004	
>=2	150	44 (29.3)	106 (70.7) 24.8 (19.4, NE)	78	40 (51.3)	38 (48.7) 4.2 (0.7, 13.6)	0.3155 (0.2002, 0.4973) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.4042
Yes	233	48 (20.6)	185 (79.4)	NE (NE, NE)	112	38 (33.9)	74 (66.1)	9.9 (6.0, NE)	0.4283 (0.2769, 0.6626) 0.0001	0.0001	
No	98	28 (28.6)	70 (71.4)	23.5 (23.5, NE)	43	24 (55.8)	19 (44.2)	6.9 (0.5, NE)	0.2772 (0.1575, 0.4879) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7800
<65	289	70 (24.2)	219 (75.8)	24.8 (23.5, NE)	126	49 (38.9)	77 (61.1)	9.9 (6.0, NE)	0.3740 (0.2557, 0.5471) <0.0001	<0.0001	
>=65	82	19 (23.2)	63 (76.8)	NE (NE, NE)	46	21 (45.7)	25 (54.3)	7.1 (0.7, NE)	0.3614 (0.1916, 0.6817) 0.0017	0.0011	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7208
<75	357	86 (24.1)	271 (75.9)	24.8 (23.5, NE)	163	65 (39.9)	98 (60.1)	9.9 (6.0, NE)	0.3726 (0.2664, 0.5211) <0.0001	<0.0001	
>=75	14	3 (21.4)	11 (78.6)	NE (3.5, NE)	9	5 (55.6)	4 (44.4)	7.1 (0.2, NE)	0.2776 (0.0655, 1.1757) 0.0818	0.0627	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.3047
White	175	32 (18.3)	143 (81.7)	NE (23.5, NE)	85	24 (28.2)	61 (71.8)	13.6 (6.9, NE)	0.4199 (0.2418, 0.7291) 0.0021	0.0016	
Non-White	196	57 (29.1)	139 (70.9)	24.8 (19.4, NE)	86	46 (53.5)	40 (46.5)	3.5 (0.5, NE)	0.3128 (0.2091, 0.4680) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.1048
Asia	147	48 (32.7)	99 (67.3)	24.8 (12.9, NE)	63	41 (65.1)	22 (34.9)	0.5 (0.3, 4.2)	0.2611 (0.1693, 0.4029) <0.0001	<0.0001	
North America	58	14 (24.1)	44 (75.9)	NE (NE, NE)	28	12 (42.9)	16 (57.1)	6.0 (1.0, NE)	0.3406 (0.1526, 0.7601) 0.0085	0.0064	
Europe + Israel	166	27 (16.3)	139 (83.7)	NE (23.5, NE)	81	17 (21.0)	64 (79.0)	13.6 (7.2, NE)	0.5243 (0.2795, 0.9835) 0.0443	0.0418	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											
0	199	47 (23.6)	152 (76.4)	NE (NE, NE)	95	35 (36.8)	60 (63.2)	13.6 (7.1, NE)	0.4201 (0.2684, 0.6575) 0.0001	0.0001	0.4863
1	172	42 (24.4)	130 (75.6)	23.5 (19.4, 24.8)	77	35 (45.5)	42 (54.5)	6.0 (0.9, NE)	0.3128 (0.1941, 0.5040) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)									0.1432
0	60 (21.7)	13 (78.3)	47 (12.5, NE)	31 (51.6)	16 (48.4)	15 (0.3, NE)	0.2369 (0.1091, 0.5144) 0.0003	<0.0001	
1	107 (25.2)	27 (74.8)	80 (NE, NE)	48 (41.7)	20 (58.3)	28 (3.3, NE)	0.4267 (0.2377, 0.7657) 0.0043	0.0034	
2	114 (26.3)	30 (73.7)	84 (19.4, NE)	50 (28.0)	14 (72.0)	36 (NE, NE)	0.6644 (0.3462, 1.2750) 0.2189	0.2300	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 (21.1)	71 (78.9)	NE (24.8, NE)	43 (46.5)	23 (53.5)	7.1 (0.5, 9.9)	0.2405 (0.1216, 0.4755) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.1298
PD	173	42 (24.3)	131 (75.7)	NE (23.5, NE)	77	28 (36.4)	49 (63.6)	NE (6.9, NE)	0.4456 (0.2718, 0.7305) 0.0014	0.0011	
PR	48	12 (25.0)	36 (75.0)	24.8 (19.4, 24.8)	21	13 (61.9)	8 (38.1)	0.5 (0.3, NE)	0.1778 (0.0758, 0.4168) 0.0001	<0.0001	
SD	82	19 (23.2)	63 (76.8)	NE (NE, NE)	54	20 (37.0)	34 (63.0)	9.9 (3.3, NE)	0.4829 (0.2550, 0.9143) 0.0254	0.0216	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.8735
Yes	37	10 (27.0)	27 (73.0)	NE (NE, NE)	13	6 (46.2)	7 (53.8)	NE (0.3, NE)	0.4595 (0.1651, 1.2790)	0.1363	
No	334	79 (23.7)	255 (76.3)	24.8 (23.5, NE)	159	64 (40.3)	95 (59.7)	9.9 (6.9, NE)	0.1365 (0.2530, 0.5027)	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.2347
Yes	24	8 (33.3)	16 (66.7)	NE (0.5, NE)	7	2 (28.6)	5 (71.4)	NE (0.3, NE)	1.2727 (0.2694, 6.0115) 0.7608	0.7638	
No	347	81 (23.3)	266 (76.7)	24.8 (23.5, NE)	165	68 (41.2)	97 (58.8)	7.2 (6.0, NE)	0.3402 (0.2432, 0.4760) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.9003
Normal Function	201	46 (22.9)	155 (77.1)	NE (NE, NE)	80	31 (38.8)	49 (61.3)	6.9 (6.0, NE)	0.3520 (0.2189, 0.5659) <0.0001	<0.0001	
Mild Impairment	123	32 (26.0)	91 (74.0)	24.8 (23.5, NE)	65	25 (38.5)	40 (61.5)	NE (1.2, NE)	0.4815 (0.2811, 0.8247) 0.0078	0.0079	
Moderate Impairment	41	11 (26.8)	30 (73.2)	19.4 (10.6, NE)	23	12 (52.2)	11 (47.8)	7.2 (0.9, NE)	0.3084 (0.1315, 0.7229) 0.0068	0.0045	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.0119
Normal Function	170	31 (18.2)	139 (81.8)	24.8 (23.5, NE)	88	39 (44.3)	49 (55.7)	9.9 (3.3, NE)	0.2350 (0.1426, 0.3871) <0.0001	<0.0001	
Mild Impairment	194	57 (29.4)	137 (70.6)	NE (12.9, NE)	82	30 (36.6)	52 (63.4)	7.2 (6.0, NE)	0.5174 (0.3277, 0.8170) 0.0047	0.0046	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.5002
Yes	331	79 (23.9)	252 (76.1)	24.8 (23.5, NE)	146	58 (39.7)	88 (60.3)	9.9 (6.9, NE)	0.3848 (0.2711, 0.5461) <0.0001	<0.0001	
No	40	10 (25.0)	30 (75.0)	NE (12.5, NE)	26	12 (46.2)	14 (53.8)	4.2 (0.5, NE)	0.2644 (0.1044, 0.6694) 0.0050	0.0029	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.3416
Positive	329	76 (23.1)	253 (76.9)	24.8 (23.5, NE)	152	62 (40.8)	90 (59.2)	9.9 (6.0, NE)	0.3464 (0.2446, 0.4906) <0.0001	<0.0001	
Negative	42	13 (31.0)	29 (69.0)	19.4 (7.6, NE)	20	8 (40.0)	12 (60.0)	3.3 (0.7, NE)	0.5186 (0.2044, 1.3156) 0.1668	0.1480	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.7697
Positive	331	77 (23.3)	254 (76.7)	24.8 (23.5, NE)	155	62 (40.0)	93 (60.0)	9.9 (6.9, NE)	0.3537 (0.2497, 0.5011) <0.0001	<0.0001	
Negative	40	12 (30.0)	28 (70.0)	NE (7.6, NE)	17	8 (47.1)	9 (52.9)	2.4 (0.5, NE)	0.4202 (0.1644, 1.0740) 0.0702	0.0591	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.9514
HER2 IHC 1+	214	17 (7.9)	197 (92.1)	NE (NE, NE)	100	27 (27.0)	73 (73.0)	NE (NE, NE)	0.2170 (0.1174, 0.4013) <0.0001	<0.0001	
HER2 IHC 2+/ISH Negative	157	14 (8.9)	143 (91.1)	NE (24.8, NE)	72	22 (30.6)	50 (69.4)	NE (6.9, NE)	0.2011 (0.1002, 0.4036) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.3733
1	220	17 (7.7)	203 (92.3)	NE (NE, NE)	94	21 (22.3)	73 (77.7)	NE (9.9, NE)	0.2550 (0.1332, 0.4883)	<0.0001	
>=2	150	14 (9.3)	136 (90.7)	NE (24.8, NE)	78	28 (35.9)	50 (64.1)	NE (4.2, NE)	0.1772 (0.0911, 0.3446)	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.0867
Yes	233	22 (9.4)	211 (90.6)	NE (NE, NE)	112	28 (25.0)	84 (75.0)	NE (9.9, NE)	0.2860 (0.1623, 0.5039) <0.0001	<0.0001	
No	98	8 (8.2)	90 (91.8)	NE (24.8, NE)	43	18 (41.9)	25 (58.1)	NE (0.5, NE)	0.1163 (0.0482, 0.2807) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.6418
<65	289	24 (8.3)	265 (91.7)	NE (24.8, NE)	126	37 (29.4)	89 (70.6)	NE (9.9, NE)	0.1905 (0.1120, 0.3240) <0.0001	<0.0001	
>=65	82	7 (8.5)	75 (91.5)	NE (NE, NE)	46	12 (26.1)	34 (73.9)	NE (6.9, NE)	0.2717 (0.1065, 0.6931) 0.0064	0.0037	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1475
<75	357	31 (8.7)	326 (91.3)	NE (24.8, NE)	163	46 (28.2)	117 (71.8)	NE (9.9, NE)	0.2170 (0.1359, 0.3465) <0.0001	<0.0001	
>=75	14	0	14 (100)	NE (NE, NE)	9	3 (33.3)	6 (66.7)	NE (0.2, NE)	0.0000 (0.0000, ) 0.9973	0.0215	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.8847
White	175	5 (2.9)	170 (97.1)	NE (NE, NE)	85	11 (12.9)	74 (87.1)	NE (NE, NE)	0.1685 (0.0577, 0.4922) 0.0011	0.0002	
Non-White	196	26 (13.3)	170 (86.7)	NE (24.8, NE)	86	38 (44.2)	48 (55.8)	9.9 (1.2, NE)	0.1935 (0.1159, 0.3231) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.0130
Asia	147	23 (15.6)	124 (84.4)	NE (24.8, NE)	63	36 (57.1)	27 (42.9)	0.9 (0.5, NE)	0.1554 (0.0906, 0.2666) <0.0001	<0.0001	
North America	58	1 (1.7)	57 (98.3)	NE (NE, NE)	28	9 (32.1)	19 (67.9)	NE (2.4, NE)	0.0420 (0.0053, 0.3326) 0.0027	<0.0001	
Europe + Israel	166	7 (4.2)	159 (95.8)	NE (NE, NE)	81	4 (4.9)	77 (95.1)	NE (NE, NE)	0.6163 (0.1761, 2.1575) 0.4490	0.4454	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											
0	199	18 (9.0)	181 (91.0)	NE (NE, NE)	95	24 (25.3)	71 (74.7)	NE (9.9, NE)	0.2583 (0.1390, 0.4797)	<0.0001	0.4094
1	172	13 (7.6)	159 (92.4)	24.8 (NE, NE)	77	25 (32.5)	52 (67.5)	NE (6.9, NE)	0.1630 (0.0809, 0.3282)	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.4682
0	60	2 (3.3)	58 (96.7)	NE (NE, NE)	31	9 (29.0)	22 (71.0)	NE (6.9, NE)	0.0846 (0.0179, 0.4003) 0.0018	<0.0001	
1	107	9 (8.4)	98 (91.6)	NE (NE, NE)	48	13 (27.1)	35 (72.9)	NE (NE, NE)	0.2508 (0.1068, 0.5893) 0.0015	0.0006	
2	114	11 (9.6)	103 (90.4)	NE (NE, NE)	50	12 (24.0)	38 (76.0)	NE (NE, NE)	0.2994 (0.1305, 0.6865) 0.0044	0.0029	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	9 (10.0)	81 (90.0)	NE (24.8, NE)	43	15 (34.9)	28 (65.1)	9.9 (9.9, NE)	0.1677 (0.0692, 0.4065) 0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.0682
PD	173	8 (4.6)	165 (95.4)	NE (NE, NE)	77	18 (23.4)	59 (76.6)	NE (NE, NE)	0.1598 (0.0690, 0.3702)	<0.0001	
PR	48	5 (10.4)	43 (89.6)	24.8 (NE, NE)	21	10 (47.6)	11 (52.4)	NE (0.3, NE)	0.1162 (0.0362, 0.3733)	<0.0001	
SD	82	13 (15.9)	69 (84.1)	NE (NE, NE)	54	16 (29.6)	38 (70.4)	NE (9.9, NE)	0.3947 (0.1877, 0.8299)	0.0112	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.8408
Yes	37	4 (10.8)	33 (89.2)	NE (NE, NE)	13	5 (38.5)	8 (61.5)	NE (0.3, NE)	0.1752 (0.0418, 0.7352)	0.0080	
No	334	27 (8.1)	307 (91.9)	NE (24.8, NE)	159	44 (27.7)	115 (72.3)	NE (9.9, NE)	0.2090 (0.1279, 0.3417)	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.5808
Yes	24	3 (12.5)	21 (87.5)	NE (NE, NE)	7	2 (28.6)	5 (71.4)	NE (0.3, NE)	0.2781 (0.0391, 1.9774) 0.2010	0.1731	
No	347	28 (8.1)	319 (91.9)	NE (24.8, NE)	165	47 (28.5)	118 (71.5)	NE (9.9, NE)	0.2018 (0.1249, 0.3260) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.1691
Normal Function	201	14 (7.0)	187 (93.0)	NE (NE, NE)	80	22 (27.5)	58 (72.5)	9.9 (6.9, NE)	0.1661 (0.0827, 0.3335) <0.0001	<0.0001	
Mild Impairment	123	16 (13.0)	107 (87.0)	24.8 (24.8, NE)	65	18 (27.7)	47 (72.3)	NE (NE, NE)	0.3424 (0.1720, 0.6816) 0.0023	0.0016	
Moderate Impairment	41	1 (2.4)	40 (97.6)	NE (NE, NE)	23	7 (30.4)	16 (69.6)	NE (2.4, NE)	0.0679 (0.0083, 0.5531) 0.0120	0.0009	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1861
Normal Function	170	14 (8.2)	156 (91.8)	NE (24.8, NE)	88	30 (34.1)	58 (65.9)	NE (6.9, NE)	0.1626 (0.0839, 0.3148) <0.0001	<0.0001	
Mild Impairment	194	17 (8.8)	177 (91.2)	NE (NE, NE)	82	18 (22.0)	64 (78.0)	NE (NE, NE)	0.2960 (0.1510, 0.5803) 0.0004	0.0002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.4421
Yes	331	28 (8.5)	303 (91.5)	NE (24.8, NE)	146	40 (27.4)	106 (72.6)	NE (9.9, NE)	0.2246 (0.1370, 0.3683) <0.0001	<0.0001	
No	40	3 (7.5)	37 (92.5)	NE (NE, NE)	26	9 (34.6)	17 (65.4)	NE (3.3, NE)	0.1184 (0.0304, 0.4612) 0.0021	0.0004	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.4363
Positive	329	30 (9.1)	299 (90.9)	NE (24.8, NE)	152	45 (29.6)	107 (70.4)	NE (9.9, NE)	0.2164 (0.1348, 0.3474) <0.0001	<0.0001	
Negative	42	1 (2.4)	41 (97.6)	NE (NE, NE)	20	4 (20.0)	16 (80.0)	NE (3.3, NE)	0.0951 (0.0105, 0.8637) 0.0366	0.0099	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Investigations; PT: Neutrophil count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.5472
Positive	331	30 (9.1)	301 (90.9)	NE (24.8, NE)	155	46 (29.7)	109 (70.3)	NE (9.9, NE)	0.2143 (0.1338, 0.3434)	<0.0001	
Negative	40	1 (2.5)	39 (97.5)	NE (NE, NE)	17	3 (17.6)	14 (82.4)	NE (2.4, NE)	0.1224 (0.0126, 1.1886)	0.0314	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.6003
HER2 IHC 1+	214	15 (7.0)	199 (93.0)	NE (NE, NE)	100	20 (20.0)	80 (80.0)	NE (10.4, NE)	0.2338 (0.1157, 0.4724) 0.0001	<0.0001	
HER2 IHC 2+/ISH Negative	157	10 (6.4)	147 (93.6)	NE (24.8, NE)	72	10 (13.9)	62 (86.1)	NE (NE, NE)	0.3169 (0.1265, 0.7941) 0.0142	0.0099	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.5022
1	220	11 (5.0)	209 (95.0)	NE (NE, NE)	94	10 (10.6)	84 (89.4)	NE (10.4, NE)	0.3328 (0.1377, 0.8045) 0.0146	0.0106	
>=2	150	14 (9.3)	136 (90.7)	NE (24.8, NE)	78	20 (25.6)	58 (74.4)	NE (NE, NE)	0.2346 (0.1133, 0.4859) 0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.4113
Yes	233	13 (5.6)	220 (94.4)	NE (NE, NE)	112	13 (11.6)	99 (88.4)	NE (NE, NE)	0.3677 (0.1675, 0.8073) 0.0126	0.0097	
No	98	8 (8.2)	90 (91.8)	NE (24.8, NE)	43	11 (25.6)	32 (74.4)	NE (10.4, NE)	0.2071 (0.0792, 0.5413) 0.0013	0.0004	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0971
<65	289	16 (5.5)	273 (94.5)	NE (24.8, NE)	126	23 (18.3)	103 (81.7)	NE (NE, NE)	0.1966 (0.0996, 0.3880) <0.0001	<0.0001	
>=65	82	9 (11.0)	73 (89.0)	NE (NE, NE)	46	7 (15.2)	39 (84.8)	NE (10.4, NE)	0.5596 (0.2054, 1.5244) 0.2562	0.2506	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5090
<75	357	24 (6.7)	333 (93.3)	NE (24.8, NE)	163	29 (17.8)	134 (82.2)	NE (NE, NE)	0.2548 (0.1444, 0.4496) <0.0001	<0.0001	
>=75	14	1 (7.1)	13 (92.9)	NE (NE, NE)	9	1 (11.1)	8 (88.9)	NE (10.4, NE)	0.6944 (0.0433, 11.1240) 0.7966	0.7955	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.7048
White	175	7 (4.0)	168 (96.0)	NE (NE, NE)	85	8 (9.4)	77 (90.6)	NE (NE, NE)	0.3020 (0.1061, 0.8599) 0.0249	0.0185	
Non-White	196	18 (9.2)	178 (90.8)	NE (24.8, NE)	86	22 (25.6)	64 (74.4)	NE (10.4, NE)	0.2379 (0.1234, 0.4584) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.9264
Asia	147	17 (11.6)	130 (88.4)	NE (24.8, NE)	63	20 (31.7)	43 (68.3)	NE (7.6, NE)	0.2261 (0.1141, 0.4479) <0.0001	<0.0001	
North America	58	3 (5.2)	55 (94.8)	NE (NE, NE)	28	4 (14.3)	24 (85.7)	NE (NE, NE)	0.2736 (0.0574, 1.3047) 0.1039	0.0850	
Europe + Israel	166	5 (3.0)	161 (97.0)	NE (NE, NE)	81	6 (7.4)	75 (92.6)	NE (NE, NE)	0.3032 (0.0901, 1.0199) 0.0538	0.0422	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 18:59; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_AESEVSOCPT10PAT\_2\_SAS.rtf

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DE.T.4.12.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.5958
0	199	12 (6.0)	187 (94.0)	NE (NE, NE)	95	16 (16.8)	79 (83.2)	NE (NE, NE)	0.2399 (0.1111, 0.5181) 0.0003	<0.0001	
1	172	13 (7.6)	159 (92.4)	24.8 (19.4, 24.8)	77	14 (18.2)	63 (81.8)	NE (10.4, NE)	0.2927 (0.1307, 0.6552) 0.0028	0.0015	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 18:59; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_AESEVSOCPT10PAT\_2\_SAS.rtf

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.0075
0	60	2 (3.3)	58 (96.7)	NE (NE, NE)	31	9 (29.0)	22 (71.0)	NE (NE, NE)	0.0995 (0.0215, 0.4609)	0.0003	
1	107	6 (5.6)	101 (94.4)	NE (NE, NE)	48	9 (18.8)	39 (81.3)	NE (10.4, NE)	0.2194 (0.0770, 0.6247)	0.0019	
2	114	12 (10.5)	102 (89.5)	NE (19.4, NE)	50	3 (6.0)	47 (94.0)	NE (NE, NE)	1.1933 (0.3258, 4.3709)	0.7846	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	5 (5.6)	85 (94.4)	NE (24.8, NE)	43	9 (20.9)	34 (79.1)	NE (NE, NE)	0.1776 (0.0544, 0.5797) 0.0042	0.0013	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.1579
PD	173	8 (4.6)	165 (95.4)	NE (NE, NE)	77	16 (20.8)	61 (79.2)	NE (7.6, NE)	0.1634 (0.0683, 0.3907)	<0.0001	
PR	48	4 (8.3)	44 (91.7)	24.8 (19.4, 24.8)	21	5 (23.8)	16 (76.2)	NE (NE, NE)	0.1243 (0.0232, 0.6660)	0.0046	
SD	82	8 (9.8)	74 (90.2)	NE (NE, NE)	54	7 (13.0)	47 (87.0)	NE (10.4, NE)	0.6170 (0.2203, 1.7283)	0.3560	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.0502
Yes	37	7 (18.9)	30 (81.1)	NE (NE, NE)	13	2 (15.4)	11 (84.6)	NE (NE, NE)	1.1620 (0.2412, 5.5971)	0.8399	
No	334	18 (5.4)	316 (94.6)	NE (24.8, NE)	159	28 (17.6)	131 (82.4)	NE (NE, NE)	0.1870 (0.0993, 0.3522)	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0017
Yes	24	6 (25.0)	18 (75.0)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9951	0.1556	
No	347	19 (5.5)	328 (94.5)	NE (24.8, NE)	165	30 (18.2)	135 (81.8)	NE (NE, NE)	0.1859 (0.1007, 0.3431) <0.0001	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.3694
Normal Function	201	9 (4.5)	192 (95.5)	NE (NE, NE)	80	13 (16.3)	67 (83.8)	NE (NE, NE)	0.1876 (0.0771, 0.4562) 0.0002	<0.0001	
Mild Impairment	123	12 (9.8)	111 (90.2)	24.8 (24.8, NE)	65	10 (15.4)	55 (84.6)	NE (NE, NE)	0.4803 (0.2024, 1.1395) 0.0962	0.0934	
Moderate Impairment	41	4 (9.8)	37 (90.2)	19.4 (19.4, NE)	23	5 (21.7)	18 (78.3)	NE (7.6, NE)	0.2843 (0.0677, 1.1940) 0.0858	0.0676	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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 Run date: 13SEP2022 – 18:59; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_AESEVSOCPT10PAT\_2\_SAS.rtf

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.3787
Normal Function	170	14 (8.2)	156 (91.8)	NE (24.8, NE)	88	20 (22.7)	68 (77.3)	NE (NE, NE)	0.2475 (0.1199, 0.5108) 0.0002	<0.0001	
Mild Impairment	194	11 (5.7)	183 (94.3)	NE (NE, NE)	82	9 (11.0)	73 (89.0)	NE (10.4, NE)	0.3376 (0.1352, 0.8430) 0.0200	0.0154	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1732
Yes	331	22 (6.6)	309 (93.4)	NE (24.8, NE)	146	22 (15.1)	124 (84.9)	NE (NE, NE)	0.3184 (0.1729, 0.5866) 0.0002	0.0001	
No	40	3 (7.5)	37 (92.5)	NE (19.4, NE)	26	8 (30.8)	18 (69.2)	NE (0.5, NE)	0.1125 (0.0233, 0.5428) 0.0065	0.0013	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.7568
Positive	329	20 (6.1)	309 (93.9)	NE (24.8, NE)	152	25 (16.4)	127 (83.6)	NE (NE, NE)	0.2574 (0.1398, 0.4737) <0.0001	<0.0001	
Negative	42	5 (11.9)	37 (88.1)	19.4 (19.4, NE)	20	5 (25.0)	15 (75.0)	NE (0.9, NE)	0.2727 (0.0651, 1.1417) 0.0753	0.0559	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: White blood cell count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.2657
Positive	331	22 (6.6)	309 (93.4)	NE (24.8, NE)	155	24 (15.5)	131 (84.5)	NE (NE, NE)	0.2890 (0.1575, 0.5303) 0.0001	<0.0001	
Negative	40	3 (7.5)	37 (92.5)	NE (NE, NE)	17	6 (35.3)	11 (64.7)	NE (0.5, NE)	0.1245 (0.0251, 0.6180) 0.0108	0.0025	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.2457
HER2 IHC 1+	214	10 (4.7)	204 (95.3)	NE (NE, NE)	100	0	100 (100)	NE (NE, NE)	NE (NE, NE) 0.9942	0.0934	
HER2 IHC 2+/ISH Negative	157	10 (6.4)	147 (93.6)	NE (NE, NE)	72	1 (1.4)	71 (98.6)	NE (NE, NE)	4.1663 (0.5306, 32.7147) 0.1747	0.1407	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.3119
1	220	9 (4.1)	211 (95.9)	NE (NE, NE)	94	0	94 (100)	NE (NE, NE)	NE (NE, NE) 0.9942	0.0909	
>=2	150	11 (7.3)	139 (92.7)	NE (NE, NE)	78	1 (1.3)	77 (98.7)	NE (NE, NE)	4.4261 (0.5626, 34.8217) 0.1575	0.1233	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.9997
Yes	233	9 (3.9)	224 (96.1)	NE (NE, NE)	112	0	112 (100)	NE (NE, NE)	NE (NE, NE) 0.9934	0.0423	
No	98	9 (9.2)	89 (90.8)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9943	0.1012	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.5952
<65	289	18 (6.2)	271 (93.8)	NE (NE, NE)	126	1 (0.8)	125 (99.2)	NE (NE, NE)	5.6697 (0.7486, 42.9425) 0.0930	0.0583	
>=65	82	2 (2.4)	80 (97.6)	NE (NE, NE)	46	0	46 (100)	NE (NE, NE)	NE (NE, NE) 0.9967	0.2865	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.12.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9996
<75	357	20 (5.6)	337 (94.4)	NE (NE, NE)	163	1 (0.6)	162 (99.4)	NE (NE, NE)	6.9041 (0.9186, 51.8924) 0.0605	0.0294	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.4418
White	175	5 (2.9)	170 (97.1)	NE (NE, NE)	85	0	85 (100)	NE (NE, NE)	NE (NE, NE) 0.9953	0.1496	
Non-White	196	15 (7.7)	181 (92.3)	NE (NE, NE)	86	1 (1.2)	85 (98.8)	NE (NE, NE)	4.9294 (0.6447, 37.6899) 0.1243	0.0888	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.7338
Asia	147	15 (10.2)	132 (89.8)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (NE, NE)	4.7808 (0.6253, 36.5514) 0.1317	0.0964	
North America	58	1 (1.7)	57 (98.3)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9978	0.4872	
Europe + Israel	166	4 (2.4)	162 (97.6)	NE (NE, NE)	81	0	81 (100)	NE (NE, NE)	NE (NE, NE) 0.9958	0.2042	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.1241
0	199	14 (7.0)	185 (93.0)	NE (NE, NE)	95	0	95 (100)	NE (NE, NE)	NE (NE, NE) 0.9924	0.0231	
1	172	6 (3.5)	166 (96.5)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	2.1035 (0.2481, 17.8321) 0.4953	0.4858	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.2635
0	60	2 (3.3)	58 (96.7)	NE (NE, NE)	31	1 (3.2)	30 (96.8)	NE (NE, NE)	1.0338 (0.0937, 11.4012) 0.9783	0.9818	
1	107	4 (3.7)	103 (96.3)	NE (NE, NE)	48	0	48 (100)	NE (NE, NE)	NE (NE, NE) 0.9958	0.2186	
2	114	9 (7.9)	105 (92.1)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	NE (NE, NE) 0.9943	0.0935	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	5 (5.6)	85 (94.4) NE (NE, NE)	43	0	43 (100) NE (NE, NE)	NE (NE, NE) 0.9957	0.1961	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 18:59; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_AESEVSOCPT10PAT\_2\_SAS.rtf

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.4753
PD	173	8 (4.6)	165 (95.4)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	3.1715 (0.3937, 25.5492)	0.2537	
PR	48	2 (4.2)	46 (95.8)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	0.2782 (NE, NE)	0.4733	
SD	82	5 (6.1)	77 (93.9)	NE (NE, NE)	54	0	54 (100)	NE (NE, NE)	0.9975 (NE, NE)	0.0691	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 18:59; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_AESEVSOCPT10PAT\_2\_SAS.rf

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.6261
Yes	37	3 (8.1)	34 (91.9)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9965	0.3079	
No	334	17 (5.1)	317 (94.9)	NE (NE, NE)	159	1 (0.6)	158 (99.4)	NE (NE, NE)	5.9582 (0.7846, 45.2476) 0.0845	0.0502	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										0.7068
Yes	24	2 (8.3)	22 (91.7)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9972	0.4232
No	347	18 (5.2)	329 (94.8)	NE (NE, NE)	165	1 (0.6)	164 (99.4)	NE (NE, NE)	6.3894 (0.8446, 48.3340) 0.0724	0.0395

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.1013
Normal Function	201	13 (6.5)	188 (93.5)	NE (NE, NE)	80	0	80 (100)	NE (NE, NE)	NE (NE, NE) 0.9934	0.0574	
Mild Impairment	123	6 (4.9)	117 (95.1)	NE (NE, NE)	65	0	65 (100)	NE (NE, NE)	NE (NE, NE) 0.9946	0.0913	
Moderate Impairment	41	1 (2.4)	40 (97.6)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	0.4781 (0.0296, 7.7115) 0.6030	0.5948	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1456
Normal Function	170	6 (3.5)	164 (96.5)	NE (NE, NE)	88	1 (1.1)	87 (98.9)	NE (NE, NE)	2.4267 (0.2885, 20.4122) 0.4145	0.3999	
Mild Impairment	194	14 (7.2)	180 (92.8)	NE (NE, NE)	82	0	82 (100)	NE (NE, NE)	NE (NE, NE) 0.9927	0.0330	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.0984
Yes	331	16 (4.8)	315 (95.2)	NE (NE, NE)	146	0	146 (100)	NE (NE, NE)	NE (NE, NE) 0.9920	0.0184	
No	40	4 (10.0)	36 (90.0)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	1.6600 (0.1730, 15.9267) 0.6605	0.6574	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.0404
Positive	329	18 (5.5)	311 (94.5)	NE (NE, NE)	152	0	152 (100)	NE (NE, NE)	NE (NE, NE) 0.9914	0.0111	
Negative	42	2 (4.8)	40 (95.2)	NE (NE, NE)	20	1 (5.0)	19 (95.0)	NE (NE, NE)	0.4755 (0.0297, 7.6035) 0.5991	0.5907	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: Platelet count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.0344
Positive	331	18 (5.4)	313 (94.6)	NE (NE, NE)	155	0	155 (100)	NE (NE, NE)	NE (NE, NE) 0.9914	0.0105	
Negative	40	2 (5.0)	38 (95.0)	NE (NE, NE)	17	1 (5.9)	16 (94.1)	NE (NE, NE)	0.4230 (0.0264, 6.7645) 0.5430	0.5304	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.7185
HER2 IHC 1+	214	9 (4.2)	205 (95.8)	NE (NE, NE)	100	3 (3.0)	97 (97.0)	NE (NE, NE)	0.9140 (0.2387, 3.4994) 0.8956	0.8937	
HER2 IHC 2+/ISH Negative	157	9 (5.7)	148 (94.3)	NE (24.8, NE)	72	2 (2.8)	70 (97.2)	NE (NE, NE)	1.2711 (0.2653, 6.0890) 0.7641	0.7635	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 18:59; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_AESEVSOCPT10PAT\_2\_SAS.rtf

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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.4432
1	220	7 (3.2)	213 (96.8)	NE (NE, NE)	94	1 (1.1)	93 (98.9)	NE (NE, NE)	2.1676 (0.2634, 17.8398) 0.4719	0.4611	
>=2	150	11 (7.3)	139 (92.7)	NE (24.8, NE)	78	4 (5.1)	74 (94.9)	NE (7.2, NE)	0.8055 (0.2428, 2.6731) 0.7238	0.7225	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.0289
Yes	233	5 (2.1)	228 (97.9)	NE (NE, NE)	112	3 (2.7)	109 (97.3)	NE (NE, NE)	0.5333 (0.1222, 2.3278) 0.4030	0.3960	
No	98	8 (8.2)	90 (91.8)	NE (24.8, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9948	0.1381	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9376
<65	289	12 (4.2)	277 (95.8)	NE (24.8, NE)	126	3 (2.4)	123 (97.6)	NE (NE, NE)	0.9761 (0.2636, 3.6143) 0.9711	0.9709	
>=65	82	6 (7.3)	76 (92.7)	NE (NE, NE)	46	2 (4.3)	44 (95.7)	NE (NE, NE)	1.4383 (0.2884, 7.1744) 0.6575	0.6557	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1564
<75	357	16 (4.5)	341 (95.5)	NE (24.8, NE)	163	5 (3.1)	158 (96.9)	NE (NE, NE)	0.8776 (0.3113, 2.4739) 0.8049	0.8043	
>=75	14	2 (14.3)	12 (85.7)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9978	0.2419	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.9590
White	175	7 (4.0)	168 (96.0)	NE (NE, NE)	85	2 (2.4)	83 (97.6)	NE (NE, NE)	1.0364 (0.2080, 5.1650) 0.9652	0.9649	
Non-White	196	11 (5.6)	185 (94.4)	NE (24.8, NE)	86	3 (3.5)	83 (96.5)	NE (NE, NE)	1.0644 (0.2877, 3.9379) 0.9255	0.9260	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.9115
Asia	147	9 (6.1)	138 (93.9)	NE (24.8, NE)	63	2 (3.2)	61 (96.8)	NE (NE, NE)	1.2503 (0.2611, 5.9876) 0.7799	0.7801	
North America	58	5 (8.6)	53 (91.4)	NE (NE, NE)	28	2 (7.1)	26 (92.9)	NE (6.0, NE)	0.5541 (0.0999, 3.0742) 0.4994	0.4940	
Europe + Israel	166	4 (2.4)	162 (97.6)	NE (NE, NE)	81	1 (1.2)	80 (98.8)	NE (NE, NE)	1.5191 (0.1655, 13.9432) 0.7116	0.7101	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.9173
0	199	7 (3.5)	192 (96.5)	NE (NE, NE)	95	2 (2.1)	93 (97.9)	NE (NE, NE)	0.9476 (0.1907, 4.7096)	0.9476	
1	172	11 (6.4)	161 (93.6)	24.8 (NE, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	1.1508 (0.3113, 4.2549)	0.8342	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.2797
0	60	6 (10.0)	54 (90.0)	NE (NE, NE)	31	2 (6.5)	29 (93.5)	NE (NE, NE)	0.9064 (0.1735, 4.7360) 0.9073	0.9073	
1	107	4 (3.7)	103 (96.3)	NE (NE, NE)	48	1 (2.1)	47 (97.9)	NE (NE, NE)	1.3177 (0.1455, 11.9340) 0.8062	0.8055	
2	114	5 (4.4)	109 (95.6)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	NE (NE, NE) 0.9954	0.1812	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	3 (3.3)	87 (96.7)	NE (24.8, NE)	43	2 (4.7)	41 (95.3)	NE (6.0, NE)	0.3473 (0.0458, 2.6341) 0.3063	0.2865	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.3902
PD	173	11 (6.4)	162 (93.6)	NE (NE, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	1.6936 (0.3668, 7.8206)	0.4962	
PR	48	1 (2.1)	47 (97.9)	24.8 (NE, NE)	21	1 (4.8)	20 (95.2)	NE (NE, NE)	0.4997 (0.0000, )	0.1061	
SD	82	6 (7.3)	76 (92.7)	NE (NE, NE)	54	1 (1.9)	53 (98.1)	NE (NE, NE)	2.7544 (0.3251, 23.3383)	0.3332	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.1750
Yes	37	4 (10.8)	33 (89.2)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9961	0.2720	
No	334	14 (4.2)	320 (95.8)	NE (24.8, NE)	159	5 (3.1)	154 (96.9)	NE (NE, NE)	0.7806 (0.2712, 2.2468) 0.6461	0.6447	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.2402
Yes	24	3 (12.5)	21 (87.5)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9967	0.3539	
No	347	15 (4.3)	332 (95.7)	NE (24.8, NE)	165	5 (3.0)	160 (97.0)	NE (NE, NE)	0.8454 (0.2973, 2.4042) 0.7528	0.7519	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.9434
Normal Function	201	6 (3.0)	195 (97.0)	NE (NE, NE)	80	1 (1.3)	79 (98.8)	NE (NE, NE)	1.1887 (0.1383, 10.2194) 0.8749	0.8747	
Mild Impairment	123	10 (8.1)	113 (91.9)	24.8 (24.8, NE)	65	2 (3.1)	63 (96.9)	NE (NE, NE)	2.0001 (0.4260, 9.3916) 0.3797	0.3717	
Moderate Impairment	41	2 (4.9)	39 (95.1)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (7.2, NE)	0.8407 (0.0759, 9.3140) 0.8876	0.8874	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.6104
Normal Function	170	8 (4.7)	162 (95.3)	NE (24.8, NE)	88	3 (3.4)	85 (96.6)	NE (NE, NE)	0.8247 (0.2080, 3.2700) 0.7839	0.7827	
Mild Impairment	194	10 (5.2)	184 (94.8)	NE (NE, NE)	82	2 (2.4)	80 (97.6)	NE (7.2, NE)	1.3976 (0.2989, 6.5338) 0.6705	0.6693	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1490
Yes	331	16 (4.8)	315 (95.2)	NE (24.8, NE)	146	3 (2.1)	143 (97.9)	NE (NE, NE)	1.6364 (0.4688, 5.7118) 0.4400	0.4360	
No	40	2 (5.0)	38 (95.0)	NE (NE, NE)	26	2 (7.7)	24 (92.3)	NE (NE, NE)	0.1770 (0.0180, 1.7435) 0.1379	0.1144	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.5740
Positive	329	13 (4.0)	316 (96.0)	NE (24.8, NE)	152	3 (2.0)	149 (98.0)	NE (NE, NE)	1.2124 (0.3350, 4.3876) 0.7692	0.7691	
Negative	42	5 (11.9)	37 (88.1)	NE (NE, NE)	20	2 (10.0)	18 (90.0)	NE (NE, NE)	0.7665 (0.1372, 4.2802) 0.7618	0.7612	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Lymphocyte count decreased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.6350
Positive	331	12 (3.6)	319 (96.4)	NE (24.8, NE)	155	3 (1.9)	152 (98.1)	NE (NE, NE)	1.1003 (0.2994, 4.0437)	0.8858	
Negative	40	6 (15.0)	34 (85.0)	NE (NE, NE)	17	2 (11.8)	15 (88.2)	NE (NE, NE)	0.8294 (0.1569, 4.3826)	0.8254	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.2556
HER2 IHC 1+	214	6 (2.8)	208 (97.2)	NE (NE, NE)	100	6 (6.0)	94 (94.0)	NE (NE, NE)	0.3897 (0.1236, 1.2291) 0.1078	0.0958	
HER2 IHC 2+/ISH Negative	157	6 (3.8)	151 (96.2)	NE (NE, NE)	72	2 (2.8)	70 (97.2)	NE (NE, NE)	1.2643 (0.2543, 6.2859) 0.7744	0.7759	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.3377
1	220	7 (3.2)	213 (96.8)	NE (NE, NE)	94	6 (6.4)	88 (93.6)	NE (NE, NE)	0.4332 (0.1443, 1.3005) 0.1358	0.1248	
>=2	150	5 (3.3)	145 (96.7)	NE (NE, NE)	78	2 (2.6)	76 (97.4)	NE (NE, NE)	1.1707 (0.2261, 6.0625) 0.8510	0.8518	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.4451
Yes	233	8 (3.4)	225 (96.6)	NE (NE, NE)	112	7 (6.3)	105 (93.8)	NE (NE, NE)	0.4449 (0.1589, 1.2458) 0.1232	0.1131	
No	98	3 (3.1)	95 (96.9)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	1.3178 (0.1371, 12.6682) 0.8111	0.8105	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.8744
<65	289	10 (3.5)	279 (96.5)	NE (NE, NE)	126	6 (4.8)	120 (95.2)	NE (NE, NE)	0.6311 (0.2269, 1.7552) 0.3778	0.3696	
>=65	82	2 (2.4)	80 (97.6)	NE (NE, NE)	46	2 (4.3)	44 (95.7)	NE (NE, NE)	0.5348 (0.0753, 3.7979) 0.5315	0.5277	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2219
<75	357	11 (3.1)	346 (96.9)	NE (NE, NE)	163	8 (4.9)	155 (95.1)	NE (NE, NE)	0.5492 (0.2191, 1.3766) 0.2012	0.1934	
>=75	14	1 (7.1)	13 (92.9)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9985	0.4142	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.0175
White	175	9 (5.1)	166 (94.9)	NE (NE, NE)	85	2 (2.4)	83 (97.6)	NE (NE, NE)	1.8480 (0.3955, 8.6348) 0.4350	0.4286	
Non-White	196	3 (1.5)	193 (98.5)	NE (NE, NE)	86	6 (7.0)	80 (93.0)	NE (NE, NE)	0.2050 (0.0511, 0.8223) 0.0253	0.0134	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.0251
Asia	147	3 (2.0)	144 (98.0)	NE (NE, NE)	63	6 (9.5)	57 (90.5)	NE (NE, NE)	0.1964 (0.0489, 0.7888) 0.0218	0.0108	
North America	58	3 (5.2)	55 (94.8)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9962	0.2545	
Europe + Israel	166	6 (3.6)	160 (96.4)	NE (NE, NE)	81	2 (2.5)	79 (97.5)	NE (NE, NE)	1.2085 (0.2400, 6.0855) 0.8184	0.8187	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.5394
0	199	9 (4.5)	190 (95.5)	NE (NE, NE)	95	5 (5.3)	90 (94.7)	NE (NE, NE)	0.7734 (0.2582, 2.3169) 0.6463	0.6380	
1	172	3 (1.7)	169 (98.3)	NE (NE, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	0.3395 (0.0650, 1.7720) 0.2001	0.1812	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.0035
0	60	1 (1.7)	59 (98.3)	NE (NE, NE)	31	0	31 (100)	NE (NE, NE)	NE (NE, NE) 0.9977	0.4685	
1	107	4 (3.7)	103 (96.3)	NE (NE, NE)	48	2 (4.2)	46 (95.8)	NE (NE, NE)	0.8350 (0.1528, 4.5640) 0.8352	0.8357	
2	114	7 (6.1)	107 (93.9)	NE (NE, NE)	50	1 (2.0)	49 (98.0)	NE (NE, NE)	2.6723 (0.3256, 21.9327) 0.3601	0.3426	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	0	90 (100)	NE (NE, NE)	43	5 (11.6)	38 (88.4)	NE (NE, NE)	0.0000 (0.0000, ) 0.9952	0.0004	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.0472
PD	173	8 (4.6)	165 (95.4)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	3.3141 (0.4138, 26.5417)	0.2319	
PR	48	1 (2.1)	47 (97.9)	NE (NE, NE)	21	3 (14.3)	18 (85.7)	NE (NE, NE)	0.1170 (0.0121, 1.1336)	0.0265	
SD	82	2 (2.4)	80 (97.6)	NE (NE, NE)	54	3 (5.6)	51 (94.4)	NE (NE, NE)	0.4389 (0.0733, 2.6269)	0.3545	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.1919
Yes	37	2 (5.4)	35 (94.6)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9974	0.4728	
No	334	10 (3.0)	324 (97.0)	NE (NE, NE)	159	8 (5.0)	151 (95.0)	NE (NE, NE)	0.5222 (0.2044, 1.3338) 0.1745	0.1665	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.3846
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9981	0.5892	
No	347	11 (3.2)	336 (96.8)	NE (NE, NE)	165	8 (4.8)	157 (95.2)	NE (NE, NE)	0.5651 (0.2255, 1.4161) 0.2234	0.2167	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Run date: 13SEP2022 – 18:59; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_AESEVSOCPT10PAT\_2\_SAS.rtf



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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.3938
Normal Function	201	8 (4.0)	193 (96.0)	NE (NE, NE)	80	4 (5.0)	76 (95.0)	NE (NE, NE)	0.6705 (0.1991, 2.2575) 0.5187	0.5125	
Mild Impairment	123	3 (2.4)	120 (97.6)	NE (NE, NE)	65	4 (6.2)	61 (93.8)	NE (NE, NE)	0.3682 (0.0821, 1.6522) 0.1921	0.1750	
Moderate Impairment	41	1 (2.4)	40 (97.6)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9977	0.4733	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1793
Normal Function	170	1 (0.6)	169 (99.4)	NE (NE, NE)	88	3 (3.4)	85 (96.6)	NE (NE, NE)	0.1529 (0.0158, 1.4801) 0.1049	0.0622	
Mild Impairment	194	10 (5.2)	184 (94.8)	NE (NE, NE)	82	5 (6.1)	77 (93.9)	NE (NE, NE)	0.7255 (0.2455, 2.1442) 0.5616	0.5606	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.2483
Yes	331	11 (3.3)	320 (96.7)	NE (NE, NE)	146	8 (5.5)	138 (94.5)	NE (NE, NE)	0.5326 (0.2129, 1.3322) 0.1780	0.1700	
No	40	1 (2.5)	39 (97.5)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9976	0.4142	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.2902
Positive	329	11 (3.3)	318 (96.7)	NE (NE, NE)	152	8 (5.3)	144 (94.7)	NE (NE, NE)	0.5502 (0.2198, 1.3774)	0.1949	
Negative	42	1 (2.4)	41 (97.6)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) 0.9978	0.4849	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Investigations; PT: Aspartate aminotransferase increased

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (derived)											0.3181
Positive	331	11 (3.3)	320 (96.7)	NE (NE, NE)	155	8 (5.2)	147 (94.8)	NE (NE, NE)	0.5589 (0.2232, 1.3991)	0.2071	
Negative	40	1 (2.5)	39 (97.5)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) 0.9978	0.5091	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.7118
HER2 IHC 1+	214	41 (19.2)	173 (80.8)	NE (NE, NE)	100	23 (23.0)	77 (77.0)	NE (NE, NE)	0.5999 (0.3564, 1.0099) 0.0545	0.0525	
HER2 IHC 2+/ISH Negative	157	22 (14.0)	135 (86.0)	NE (24.8, NE)	72	14 (19.4)	58 (80.6)	15.4 (15.4, NE)	0.4909 (0.2454, 0.9819) 0.0443	0.0405	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.0579
1	220	30 (13.6)	190 (86.4)	NE (NE, NE)	94	23 (24.5)	71 (75.5)	15.4 (15.4, NE)	0.3976 (0.2277, 0.6941) 0.0012	0.0008	
>=2	150	33 (22.0)	117 (78.0)	24.8 (24.8, NE)	78	14 (17.9)	64 (82.1)	NE (NE, NE)	0.8772 (0.4639, 1.6586) 0.6868	0.6874	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.8486
Yes	233	34 (14.6)	199 (85.4)	NE (NE, NE)	112	22 (19.6)	90 (80.4)	NE (15.4, NE)	0.5540 (0.3201, 0.9590) 0.0349	0.0329	
No	98	22 (22.4)	76 (77.6)	24.8 (24.8, NE)	43	11 (25.6)	32 (74.4)	NE (NE, NE)	0.5489 (0.2618, 1.1510) 0.1123	0.1076	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4623
<65	289	41 (14.2)	248 (85.8)	NE (24.8, NE)	126	24 (19.0)	102 (81.0)	NE (15.4, NE)	0.5198 (0.3094, 0.8735) 0.0135	0.0122	
>=65	82	22 (26.8)	60 (73.2)	NE (12.0, NE)	46	13 (28.3)	33 (71.7)	NE (4.3, NE)	0.7128 (0.3558, 1.4283) 0.3398	0.3362	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1007
<75	357	59 (16.5)	298 (83.5)	NE (24.8, NE)	163	36 (22.1)	127 (77.9)	NE (15.4, NE)	0.5172 (0.3377, 0.7921) 0.0024	0.0021	
>=75	14	4 (28.6)	10 (71.4)	NE (3.4, NE)	9	1 (11.1)	8 (88.9)	NE (2.3, NE)	2.6461 (0.2948, 23.7549) 0.3848	0.3663	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.5839
White	175	30 (17.1)	145 (82.9)	NE (NE, NE)	85	17 (20.0)	68 (80.0)	NE (15.4, NE)	0.6536 (0.3568, 1.1975) 0.1687	0.1658	
Non-White	196	33 (16.8)	163 (83.2)	NE (24.8, NE)	86	20 (23.3)	66 (76.7)	NE (NE, NE)	0.4814 (0.2716, 0.8531) 0.0123	0.0107	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.6746
Asia	147	22 (15.0)	125 (85.0)	NE (24.8, NE)	63	10 (15.9)	53 (84.1)	NE (NE, NE)	0.6190 (0.2865, 1.3373) 0.2223	0.2176	
North America	58	9 (15.5)	49 (84.5)	NE (NE, NE)	28	4 (14.3)	24 (85.7)	NE (NE, NE)	0.8437 (0.2540, 2.8033) 0.7815	0.7862	
Europe + Israel	166	32 (19.3)	134 (80.7)	NE (NE, NE)	81	23 (28.4)	58 (71.6)	NE (15.4, NE)	0.4982 (0.2889, 0.8591) 0.0122	0.0109	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.8236
0	199	29 (14.6)	170 (85.4)	NE (NE, NE)	95	18 (18.9)	77 (81.1)	NE (15.4, NE)	0.5285 (0.2901, 0.9630) 0.0372	0.0343	
1	172	34 (19.8)	138 (80.2)	24.8 (NE, NE)	77	19 (24.7)	58 (75.3)	NE (NE, NE)	0.5749 (0.3217, 1.0274) 0.0617	0.0593	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.7062
0	60	9 (15.0)	51 (85.0)	NE (14.6, NE)	31	8 (25.8)	23 (74.2)	NE (2.9, NE)	0.3641 (0.1290, 1.0275)	0.0471	
1	107	18 (16.8)	89 (83.2)	NE (NE, NE)	48	13 (27.1)	35 (72.9)	15.4 (15.4, NE)	0.4799 (0.2331, 0.9879)	0.0423	
2	114	24 (21.1)	90 (78.9)	NE (NE, NE)	50	11 (22.0)	39 (78.0)	NE (NE, NE)	0.7562 (0.3668, 1.5591)	0.4484	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	12 (13.3)	78 (86.7)	NE (24.8, NE)	43	5 (11.6)	38 (88.4)	NE (NE, NE)	0.6260 (0.2114, 1.8533) 0.3977	0.3942	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.12.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.3824
PD	173	31 (17.9)	142 (82.1)	NE (NE, NE)	77	18 (23.4)	59 (76.6)	NE (NE, NE)	0.5299 (0.2920, 0.9614)	0.0347	
PR	48	7 (14.6)	41 (85.4)	24.8 (NE, NE)	21	6 (28.6)	15 (71.4)	NE (0.7, NE)	0.2623 (0.0811, 0.8482)	0.0170	
SD	82	17 (20.7)	65 (79.3)	NE (NE, NE)	54	11 (20.4)	43 (79.6)	NE (15.4, NE)	0.8221 (0.3809, 1.7747)	0.6144	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.5324
Yes	37	1 (2.7)	36 (97.3)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	0.3466 (0.0217, 5.5478)	0.4343	
No	334	62 (18.6)	272 (81.4)	NE (24.8, NE)	159	36 (22.6)	123 (77.4)	NE (15.4, NE)	0.4539 (0.3832, 0.8878)	0.5833 (0.3832, 0.8878)	0.0112

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.1211
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	2 (28.6)	5 (71.4)	NE (0.3, NE)	0.1376 (0.0124, 1.5209) 0.1057	0.0583	
No	347	62 (17.9)	285 (82.1)	NE (24.8, NE)	165	35 (21.2)	130 (78.8)	NE (15.4, NE)	0.5964 (0.3902, 0.9116) 0.0170	0.0161	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.1242
Normal Function	201	25 (12.4)	176 (87.6)	NE (NE, NE)	80	17 (21.3)	63 (78.8)	NE (NE, NE)	0.4082 (0.2162, 0.7709) 0.0057	0.0045	
Mild Impairment	123	21 (17.1)	102 (82.9)	24.8 (24.8, NE)	65	14 (21.5)	51 (78.5)	15.4 (15.4, NE)	0.5342 (0.2645, 1.0790) 0.0805	0.0761	
Moderate Impairment	41	15 (36.6)	26 (63.4)	NE (5.1, NE)	23	6 (26.1)	17 (73.9)	NE (2.9, NE)	1.2026 (0.4655, 3.1069) 0.7032	0.7033	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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[c] Two-sided p-value from unstratified log-rank test.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.8014
Normal Function	170	28 (16.5)	142 (83.5)	NE (24.8, NE)	88	19 (21.6)	69 (78.4)	NE (NE, NE)	0.5093 (0.2793, 0.9288) 0.0278	0.0257	
Mild Impairment	194	33 (17.0)	161 (83.0)	NE (NE, NE)	82	18 (22.0)	64 (78.0)	NE (15.4, NE)	0.5757 (0.3207, 1.0333) 0.0643	0.0608	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.4955
Yes	331	55 (16.6)	276 (83.4)	NE (24.8, NE)	146	33 (22.6)	113 (77.4)	NE (15.4, NE)	0.5332 (0.3432, 0.8285) 0.0052	0.0046	
No	40	8 (20.0)	32 (80.0)	NE (14.6, NE)	26	4 (15.4)	22 (84.6)	NE (NE, NE)	0.7258 (0.2001, 2.6317) 0.6258	0.6142	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (XRS)											0.9980
Positive	329	55 (16.7)	274 (83.3)	NE (24.8, NE)	152	32 (21.1)	120 (78.9)	NE (15.4, NE)	0.5581 (0.3573, 0.8716)	0.0096	
Negative	42	8 (19.0)	34 (81.0)	NE (10.6, NE)	20	5 (25.0)	15 (75.0)	NE (2.9, NE)	0.5883 (0.1852, 1.8682)	0.3674	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.7435
Positive	331	57 (17.2)	274 (82.8)	NE (24.8, NE)	155	33 (21.3)	122 (78.7)	NE (15.4, NE)	0.5724 (0.3692, 0.8873)	0.0119	
Negative	40	6 (15.0)	34 (85.0)	NE (10.6, NE)	17	4 (23.5)	13 (76.5)	NE (2.9, NE)	0.4561 (0.1207, 1.7239)	0.2397	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.5343
HER2 IHC 1+	214	25 (11.7)	189 (88.3)	NE (NE, NE)	100	5 (5.0)	95 (95.0)	NE (NE, NE)	1.8346 (0.6952, 4.8410) 0.2203	0.2141	
HER2 IHC 2+/ISH Negative	157	13 (8.3)	144 (91.7)	NE (24.8, NE)	72	4 (5.6)	68 (94.4)	NE (15.4, NE)	0.9718 (0.3072, 3.0744) 0.9612	0.9601	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.2667
1	220	19 (8.6)	201 (91.4)	NE (NE, NE)	94	6 (6.4)	88 (93.6)	NE (15.4, NE)	1.0018 (0.3940, 2.5470) 0.9970	0.9983	
>=2	150	19 (12.7)	131 (87.3)	NE (24.8, NE)	78	3 (3.8)	75 (96.2)	NE (NE, NE)	2.4670 (0.7199, 8.4536) 0.1507	0.1379	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Prior CDK4/6											0.5341
Yes	233	16 (6.9)	217 (93.1)	NE (NE, NE)	112	5 (4.5)	107 (95.5)	NE (15.4, NE)	1.2664 (0.4570, 3.5091) 0.6497	0.6498	
No	98	17 (17.3)	81 (82.7)	NE (24.8, NE)	43	3 (7.0)	40 (93.0)	NE (NE, NE)	1.7429 (0.5047, 6.0188) 0.3796	0.3740	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7298
<65	289	26 (9.0)	263 (91.0)	NE (24.8, NE)	126	6 (4.8)	120 (95.2)	NE (15.4, NE)	1.3570 (0.5496, 3.3503) 0.5080	0.5055	
>=65	82	12 (14.6)	70 (85.4)	NE (NE, NE)	46	3 (6.5)	43 (93.5)	NE (NE, NE)	1.8267 (0.5087, 6.5590) 0.3556	0.3507	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Age											0.8808
<75	357	36 (10.1)	321 (89.9)	NE (24.8, NE)	163	8 (4.9)	155 (95.1)	NE (15.4, NE)	1.4890 (0.6832, 3.2452) 0.3165	0.3134	
>=75	14	2 (14.3)	12 (85.7)	NE (4.5, NE)	9	1 (11.1)	8 (88.9)	NE (2.3, NE)	1.1575 (0.1041, 12.8742) 0.9053	0.9052	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Race											0.7244
White	175	14 (8.0)	161 (92.0)	NE (NE, NE)	85	3 (3.5)	82 (96.5)	NE (15.4, NE)	1.8271 (0.5178, 6.4474) 0.3488	0.3424	
Non-White	196	24 (12.2)	172 (87.8)	NE (24.8, NE)	86	6 (7.0)	80 (93.0)	NE (NE, NE)	1.2340 (0.4962, 3.0692) 0.6510	0.6507	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.6027
Asia	147	20 (13.6)	127 (86.4)	NE (24.8, NE)	63	4 (6.3)	59 (93.7)	NE (NE, NE)	1.4619 (0.4909, 4.3537) 0.4952	0.4936	
North America	58	8 (13.8)	50 (86.2)	NE (NE, NE)	28	1 (3.6)	27 (96.4)	NE (NE, NE)	3.3037 (0.4092, 26.6705) 0.2621	0.2346	
Europe + Israel	166	10 (6.0)	156 (94.0)	NE (NE, NE)	81	4 (4.9)	77 (95.1)	NE (15.4, NE)	0.9045 (0.2766, 2.9581) 0.8681	0.8667	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.2709
0	199	18 (9.0)	181 (91.0)	NE (NE, NE)	95	6 (6.3)	89 (93.7)	NE (15.4, NE)	1.0350 (0.4055, 2.6419) 0.9426	0.9410	
1	172	20 (11.6)	152 (88.4)	24.8 (NE, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	2.2415 (0.6533, 7.6905) 0.1994	0.1883	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.9791
0	60	6 (10.0)	54 (90.0)	NE (14.6, NE)	31	2 (6.5)	29 (93.5)	NE (NE, NE)	0.9822 (0.1871, 5.1578) 0.9831	0.9832	
1	107	11 (10.3)	96 (89.7)	NE (NE, NE)	48	3 (6.3)	45 (93.8)	NE (15.4, NE)	1.4110 (0.3907, 5.0959) 0.5992	0.5973	
2	114	14 (12.3)	100 (87.7)	NE (NE, NE)	50	3 (6.0)	47 (94.0)	NE (NE, NE)	1.7199 (0.4895, 6.0434) 0.3977	0.3930	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	7 (7.8)	83 (92.2)	NE (24.8, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	1.5865 (0.1837, 13.7002) 0.6748	0.6722	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.6265
PD	173	18 (10.4)	155 (89.6)	NE (NE, NE)	77	4 (5.2)	73 (94.8)	NE (NE, NE)	1.4995 (0.4992, 4.5041)	0.4686	
PR	48	4 (8.3)	44 (91.7)	24.8 (NE, NE)	21	2 (9.5)	19 (90.5)	NE (NE, NE)	0.3791 (0.0582, 2.4683)	0.2994	
SD	82	9 (11.0)	73 (89.0)	NE (NE, NE)	54	3 (5.6)	51 (94.4)	NE (15.4, NE)	1.5754 (0.4206, 5.9007)	0.4970	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.5664
Yes	37	1 (2.7)	36 (97.3)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.5533	
No	334	37 (11.1)	297 (88.9)	NE (24.8, NE)	159	9 (5.7)	150 (94.3)	NE (15.4, NE)	1.4360 (0.6847, 3.0115) 0.3382	0.3359	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.2246
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	1 (14.3)	6 (85.7)	NE (0.7, NE)	0.2979 (0.0186, 4.7641) 0.3919	0.3631	
No	347	37 (10.7)	310 (89.3)	NE (24.8, NE)	165	8 (4.8)	157 (95.2)	NE (15.4, NE)	1.5934 (0.7330, 3.4636) 0.2396	0.2362	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.9644
Normal Function	201	15 (7.5)	186 (92.5)	NE (NE, NE)	80	3 (3.8)	77 (96.3)	NE (NE, NE)	1.4045 (0.3988, 4.9462) 0.5970	0.5950	
Mild Impairment	123	11 (8.9)	112 (91.1)	24.8 (24.8, NE)	65	3 (4.6)	62 (95.4)	15.4 (15.4, NE)	1.3363 (0.3570, 5.0018) 0.6668	0.6666	
Moderate Impairment	41	10 (24.4)	31 (75.6)	NE (12.0, NE)	23	3 (13.0)	20 (87.0)	NE (NE, NE)	1.7381 (0.4773, 6.3298) 0.4018	0.3972	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1971
Normal Function	170	15 (8.8)	155 (91.2)	NE (24.8, NE)	88	2 (2.3)	86 (97.7)	NE (NE, NE)	2.6949 (0.6049, 12.0053) 0.1934	0.1764	
Mild Impairment	194	21 (10.8)	173 (89.2)	NE (NE, NE)	82	7 (8.5)	75 (91.5)	NE (15.4, NE)	0.9422 (0.3941, 2.2524) 0.8935	0.8939	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.6092
Yes	331	32 (9.7)	299 (90.3)	NE (24.8, NE)	146	8 (5.5)	138 (94.5)	NE (15.4, NE)	1.3406 (0.6107, 2.9426) 0.4649	0.4637	
No	40	6 (15.0)	34 (85.0)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	2.2229 (0.2505, 19.7227) 0.4732	0.4638	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.12.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Anaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.6887
Positive	329	32 (9.7)	297 (90.3)	NE (24.8, NE)	152	8 (5.3)	144 (94.7)	NE (15.4, NE)	1.3618 (0.6198, 2.9921)	0.4402	
Negative	42	6 (14.3)	36 (85.7)	NE (10.6, NE)	20	1 (5.0)	19 (95.0)	NE (NE, NE)	1.9813 (0.2285, 17.1831)	0.5272	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Anaemia

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.8659
Positive	331	34 (10.3)	297 (89.7)	NE (24.8, NE)	155	8 (5.2)	147 (94.8)	NE (15.4, NE)	1.4846 (0.6795, 3.2436)	0.3183	
Negative	40	4 (10.0)	36 (90.0)	NE (10.6, NE)	17	1 (5.9)	16 (94.1)	NE (2.9, NE)	1.0049 (0.1019, 9.9149)	0.9966	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.7866
HER2 IHC 1+	214	13 (6.1)	201 (93.9)	NE (NE, NE)	100	14 (14.0)	86 (86.0)	NE (NE, NE)	0.3298 (0.1520, 0.7156) 0.0050	0.0033	
HER2 IHC 2+/ISH Negative	157	8 (5.1)	149 (94.9)	NE (NE, NE)	72	10 (13.9)	62 (86.1)	NE (NE, NE)	0.3149 (0.1231, 0.8053) 0.0159	0.0111	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.6604
1	220	11 (5.0)	209 (95.0)	NE (NE, NE)	94	13 (13.8)	81 (86.2)	NE (NE, NE)	0.2873 (0.1265, 0.6525) 0.0029	0.0016	
>=2	150	10 (6.7)	140 (93.3)	NE (NE, NE)	78	11 (14.1)	67 (85.9)	NE (NE, NE)	0.3868 (0.1627, 0.9196) 0.0316	0.0260	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.5262
Yes	233	14 (6.0)	219 (94.0)	NE (NE, NE)	112	14 (12.5)	98 (87.5)	NE (NE, NE)	0.3747 (0.1752, 0.8017) 0.0114	0.0088	
No	98	5 (5.1)	93 (94.9)	NE (NE, NE)	43	7 (16.3)	36 (83.7)	NE (NE, NE)	0.2476 (0.0776, 0.7899) 0.0183	0.0110	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4478
<65	289	13 (4.5)	276 (95.5)	NE (NE, NE)	126	16 (12.7)	110 (87.3)	NE (NE, NE)	0.2708 (0.1273, 0.5762) 0.0007	0.0003	
>=65	82	8 (9.8)	74 (90.2)	NE (NE, NE)	46	8 (17.4)	38 (82.6)	NE (NE, NE)	0.4829 (0.1808, 1.2900) 0.1465	0.1417	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Age											0.0299
<75	357	19 (5.3)	338 (94.7)	NE (NE, NE)	163	24 (14.7)	139 (85.3)	NE (NE, NE)	0.2839 (0.1534, 0.5257) 0.0001	<0.0001	
>=75	14	2 (14.3)	12 (85.7)	NE (3.4, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9978	0.2335	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.5028
White	175	13 (7.4)	162 (92.6)	NE (NE, NE)	85	13 (15.3)	72 (84.7)	NE (NE, NE)	0.3968 (0.1820, 0.8651) 0.0201	0.0162	
Non-White	196	8 (4.1)	188 (95.9)	NE (NE, NE)	86	11 (12.8)	75 (87.2)	NE (NE, NE)	0.2468 (0.0969, 0.6286) 0.0034	0.0016	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Region											0.2365
Asia	147	2 (1.4)	145 (98.6)	NE (NE, NE)	63	3 (4.8)	60 (95.2)	NE (NE, NE)	0.2795 (0.0467, 1.6731) 0.1627	0.1362	
North America	58	0	58 (100)	NE (NE, NE)	28	2 (7.1)	26 (92.9)	NE (NE, NE)	0.0000 (0.0000, ) 0.9968	0.0371	
Europe + Israel	166	19 (11.4)	147 (88.6)	NE (NE, NE)	81	19 (23.5)	62 (76.5)	NE (NE, NE)	0.3761 (0.1971, 0.7176) 0.0030	0.0022	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.6220
0	199	9 (4.5)	190 (95.5)	NE (NE, NE)	95	9 (9.5)	86 (90.5)	NE (NE, NE)	0.3576 (0.1389, 0.9204) 0.0330	0.0265	
1	172	12 (7.0)	160 (93.0)	NE (NE, NE)	77	15 (19.5)	62 (80.5)	NE (NE, NE)	0.2940 (0.1357, 0.6373) 0.0019	0.0010	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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DE.T.4.12.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.5177
0	60	3 (5.0)	57 (95.0)	NE (NE, NE)	31	6 (19.4)	25 (80.6)	NE (NE, NE)	0.2394 (0.0599, 0.9579) 0.0433	0.0282	
1	107	5 (4.7)	102 (95.3)	NE (NE, NE)	48	9 (18.8)	39 (81.3)	NE (NE, NE)	0.2058 (0.0686, 0.6177) 0.0048	0.0019	
2	114	10 (8.8)	104 (91.2)	NE (NE, NE)	50	7 (14.0)	43 (86.0)	NE (NE, NE)	0.5122 (0.1908, 1.3745) 0.1840	0.1766	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	3 (3.3)	87 (96.7)	NE (NE, NE)	43	2 (4.7)	41 (95.3)	NE (NE, NE)	0.4441 (0.0693, 2.8452) 0.3917	0.3802	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.3849
PD	173	13 (7.5)	160 (92.5)	NE (NE, NE)	77	14 (18.2)	63 (81.8)	NE (NE, NE)	0.2952 (0.1356, 0.6429)	0.0012	
PR	48	1 (2.1)	47 (97.9)	NE (NE, NE)	21	3 (14.3)	18 (85.7)	NE (NE, NE)	0.1277 (0.0132, 1.2332)	0.0353	
SD	82	6 (7.3)	76 (92.7)	NE (NE, NE)	54	6 (11.1)	48 (88.9)	NE (NE, NE)	0.6186 (0.1991, 1.9216)	0.4030	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Reported history of CNS metastases											0.2020
Yes	37	0	37 (100)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	0.0000 (0.0000, ) 0.9980	0.0916	
No	334	21 (6.3)	313 (93.7)	NE (NE, NE)	159	23 (14.5)	136 (85.5)	NE (NE, NE)	0.3494 (0.1915, 0.6378) 0.0006	0.0004	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.1762
Yes	24	0	24 (100)	NE (NE, NE)	7	1 (14.3)	6 (85.7)	NE (0.3, NE)	0.0000 (0.0000, ) 0.9983	0.0641	
No	347	21 (6.1)	326 (93.9)	NE (NE, NE)	165	23 (13.9)	142 (86.1)	NE (NE, NE)	0.3477 (0.1904, 0.6349) 0.0006	0.0003	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.1832
Normal Function	201	8 (4.0)	193 (96.0)	NE (NE, NE)	80	13 (16.3)	67 (83.8)	NE (NE, NE)	0.1914 (0.0772, 0.4746) 0.0004	<0.0001	
Mild Impairment	123	8 (6.5)	115 (93.5)	NE (NE, NE)	65	8 (12.3)	57 (87.7)	NE (NE, NE)	0.4000 (0.1455, 1.0994) 0.0757	0.0671	
Moderate Impairment	41	5 (12.2)	36 (87.8)	NE (NE, NE)	23	3 (13.0)	20 (87.0)	NE (NE, NE)	0.8244 (0.1964, 3.4604) 0.7920	0.7975	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.2713
Normal Function	170	10 (5.9)	160 (94.1)	NE (NE, NE)	88	16 (18.2)	72 (81.8)	NE (NE, NE)	0.2399 (0.1068, 0.5388) 0.0005	0.0002	
Mild Impairment	194	11 (5.7)	183 (94.3)	NE (NE, NE)	82	8 (9.8)	74 (90.2)	NE (NE, NE)	0.5062 (0.2016, 1.2710) 0.1472	0.1403	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.5229
Yes	331	20 (6.0)	311 (94.0)	NE (NE, NE)	146	21 (14.4)	125 (85.6)	NE (NE, NE)	0.3358 (0.1802, 0.6258) 0.0006	0.0003	
No	40	1 (2.5)	39 (97.5)	NE (NE, NE)	26	3 (11.5)	23 (88.5)	NE (NE, NE)	0.2083 (0.0217, 2.0028) 0.1743	0.1321	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.8237
Positive	329	19 (5.8)	310 (94.2)	NE (NE, NE)	152	21 (13.8)	131 (86.2)	NE (NE, NE)	0.3295 (0.1752, 0.6196)	0.0003	
Negative	42	2 (4.8)	40 (95.2)	NE (NE, NE)	20	3 (15.0)	17 (85.0)	NE (NE, NE)	0.3086 (0.0515, 1.8474)	0.1756	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Blood and lymphatic system disorders; PT: Neutropenia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.7080
Positive	331	19 (5.7)	312 (94.3)	NE (NE, NE)	155	21 (13.5)	134 (86.5)	NE (NE, NE)	0.3345 (0.1778, 0.6292)	0.0004	
Negative	40	2 (5.0)	38 (95.0)	NE (NE, NE)	17	3 (17.6)	14 (82.4)	NE (NE, NE)	0.2731 (0.0456, 1.6349)	0.1303	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.12.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.0462
HER2 IHC 1+	214	23 (10.7)	191 (89.3)	NE (NE, NE)	100	8 (8.0)	92 (92.0)	NE (NE, NE)	0.9831 (0.4326, 2.2341) 0.9675	0.9674	
HER2 IHC 2+/ISH Negative	157	18 (11.5)	139 (88.5)	NE (NE, NE)	72	1 (1.4)	71 (98.6)	NE (NE, NE)	6.6256 (0.8795, 49.9126) 0.0665	0.0342	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.1947
1	220	15 (6.8)	205 (93.2)	NE (NE, NE)	94	5 (5.3)	89 (94.7)	NE (NE, NE)	1.0672 (0.3841, 2.9648) 0.9007	0.9005	
>=2	150	26 (17.3)	124 (82.7)	NE (NE, NE)	78	4 (5.1)	74 (94.9)	NE (NE, NE)	2.3793 (0.8180, 6.9200) 0.1116	0.1014	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.9122
Yes	233	24 (10.3)	209 (89.7)	NE (NE, NE)	112	5 (4.5)	107 (95.5)	NE (NE, NE)	1.6422 (0.6168, 4.3724) 0.3208	0.3164	
No	98	11 (11.2)	87 (88.8)	NE (NE, NE)	43	2 (4.7)	41 (95.3)	NE (NE, NE)	2.0485 (0.4502, 9.3218) 0.3536	0.3436	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2381
<65	289	30 (10.4)	259 (89.6)	NE (NE, NE)	126	4 (3.2)	122 (96.8)	NE (NE, NE)	2.4271 (0.8464, 6.9605) 0.0990	0.0887	
>=65	82	11 (13.4)	71 (86.6)	NE (NE, NE)	46	5 (10.9)	41 (89.1)	NE (NE, NE)	1.0032 (0.3432, 2.9322) 0.9954	0.9966	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.4090
<75	357	40 (11.2)	317 (88.8)	NE (NE, NE)	163	9 (5.5)	154 (94.5)	NE (NE, NE)	1.5346 (0.7373, 3.1941) 0.2521	0.2483	
>=75	14	1 (7.1)	13 (92.9)	NE (5.9, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9985	0.4561	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.9789
White	175	18 (10.3)	157 (89.7)	NE (NE, NE)	85	4 (4.7)	81 (95.3)	NE (NE, NE)	1.5397 (0.5128, 4.6227) 0.4416	0.4380	
Non-White	196	23 (11.7)	173 (88.3)	NE (NE, NE)	86	5 (5.8)	81 (94.2)	NE (NE, NE)	1.6436 (0.6187, 4.3660) 0.3189	0.3141	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.9980
Asia	147	15 (10.2)	132 (89.8)	NE (NE, NE)	63	3 (4.8)	60 (95.2)	NE (NE, NE)	1.7848 (0.5105, 6.2396) 0.3643	0.3576	
North America	58	5 (8.6)	53 (91.4)	NE (NE, NE)	28	1 (3.6)	27 (96.4)	NE (NE, NE)	0.9070 (0.0996, 8.2574) 0.9309	0.9309	
Europe + Israel	166	21 (12.7)	145 (87.3)	NE (NE, NE)	81	5 (6.2)	76 (93.8)	NE (NE, NE)	1.6436 (0.6138, 4.4007) 0.3228	0.3181	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.1562
0	199	19 (9.5)	180 (90.5)	NE (NE, NE)	95	2 (2.1)	93 (97.9)	NE (NE, NE)	3.4429 (0.7947, 14.9154) 0.0984	0.0788	
1	172	22 (12.8)	150 (87.2)	NE (NE, NE)	77	7 (9.1)	70 (90.9)	NE (NE, NE)	1.0526 (0.4418, 2.5077) 0.9078	0.9070	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.8119
0	60	11 (18.3)	49 (81.7)	NE (NE, NE)	31	3 (9.7)	28 (90.3)	NE (NE, NE)	1.3295 (0.3601, 4.9077) 0.6691	0.6694	
1	107	9 (8.4)	98 (91.6)	NE (NE, NE)	48	3 (6.3)	45 (93.8)	NE (NE, NE)	1.2335 (0.3324, 4.5771) 0.7538	0.7542	
2	114	11 (9.6)	103 (90.4)	NE (NE, NE)	50	1 (2.0)	49 (98.0)	NE (NE, NE)	3.1545 (0.3974, 25.0420) 0.2771	0.2519	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	10 (11.1)	80 (88.9)	NE (NE, NE)	43	2 (4.7)	41 (95.3)	NE (NE, NE)	1.7758 (0.3812, 8.2717) 0.4645	0.4586	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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DE.T.4.12.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.1193
PD	173	16 (9.2)	157 (90.8)	NE (NE, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	2.8791 (0.6568, 12.6200)	0.1424	
PR	48	6 (12.5)	42 (87.5)	NE (NE, NE)	21	4 (19.0)	17 (81.0)	NE (NE, NE)	0.5363 (0.1487, 1.9341)	0.3336	
SD	82	10 (12.2)	72 (87.8)	NE (NE, NE)	54	2 (3.7)	52 (96.3)	NE (NE, NE)	2.5266 (0.5445, 11.7240)	0.2203	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.12.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.2524
Yes	37	4 (10.8)	33 (89.2)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9959	0.2369	
No	334	37 (11.1)	297 (88.9)	NE (NE, NE)	159	9 (5.7)	150 (94.3)	NE (NE, NE)	1.4512 (0.6932, 3.0384) 0.3232	0.3205	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.3227
Yes	24	3 (12.5)	21 (87.5)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9966	0.3351	
No	347	38 (11.0)	309 (89.0)	NE (NE, NE)	165	9 (5.5)	156 (94.5)	NE (NE, NE)	1.4779 (0.7073, 3.0881) 0.2988	0.2957	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.8300
Normal Function	201	20 (10.0)	181 (90.0)	NE (NE, NE)	80	5 (6.3)	75 (93.8)	NE (NE, NE)	1.1567 (0.4261, 3.1399) 0.7751	0.7746	
Mild Impairment	123	14 (11.4)	109 (88.6)	NE (NE, NE)	65	3 (4.6)	62 (95.4)	NE (NE, NE)	1.8921 (0.5345, 6.6983) 0.3228	0.3153	
Moderate Impairment	41	4 (9.8)	37 (90.2)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	1.7867 (0.1978, 16.1431) 0.6053	0.6003	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.2202
Normal Function	170	16 (9.4)	154 (90.6)	NE (NE, NE)	88	6 (6.8)	82 (93.2)	NE (NE, NE)	1.1032 (0.4264, 2.8542) 0.8395	0.8396	
Mild Impairment	194	24 (12.4)	170 (87.6)	NE (NE, NE)	82	3 (3.7)	79 (96.3)	NE (NE, NE)	2.4550 (0.7301, 8.2556) 0.1466	0.1338	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.4237
Yes	331	37 (11.2)	294 (88.8)	NE (NE, NE)	146	7 (4.8)	139 (95.2)	NE (NE, NE)	1.8442 (0.8164, 4.1657) 0.1410	0.1352	
No	40	4 (10.0)	36 (90.0)	NE (NE, NE)	26	2 (7.7)	24 (92.3)	NE (NE, NE)	0.6537 (0.1015, 4.2113) 0.6547	0.6527	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.3043
Positive	329	34 (10.3)	295 (89.7)	NE (NE, NE)	152	6 (3.9)	146 (96.1)	NE (NE, NE)	1.9730 (0.8205, 4.7443)	0.1220	
Negative	42	7 (16.7)	35 (83.3)	NE (NE, NE)	20	3 (15.0)	17 (85.0)	NE (NE, NE)	0.8642 (0.2140, 3.4899)	0.8375	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.4982
Positive	331	35 (10.6)	296 (89.4)	NE (NE, NE)	155	7 (4.5)	148 (95.5)	NE (NE, NE)	1.7692 (0.7784, 4.0211)	0.1677	
Negative	40	6 (15.0)	34 (85.0)	NE (NE, NE)	17	2 (11.8)	15 (88.2)	NE (NE, NE)	0.9376 (0.1791, 4.9078)	0.9392	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.4882
HER2 IHC 1+	214	9 (4.2)	205 (95.8)	NE (NE, NE)	100	2 (2.0)	98 (98.0)	NE (NE, NE)	1.8398 (0.3937, 8.5973) 0.4383	0.4309	
HER2 IHC 2+/ISH Negative	157	11 (7.0)	146 (93.0)	NE (NE, NE)	72	1 (1.4)	71 (98.6)	NE (NE, NE)	3.5362 (0.4493, 27.8348) 0.2302	0.2010	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.9451
1	220	7 (3.2)	213 (96.8)	NE (NE, NE)	94	1 (1.1)	93 (98.9)	NE (NE, NE)	2.6003 (0.3174, 21.3023) 0.3732	0.3545	
>=2	150	13 (8.7)	137 (91.3)	NE (NE, NE)	78	2 (2.6)	76 (97.4)	NE (NE, NE)	2.4030 (0.5311, 10.8729) 0.2550	0.2406	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.12.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.3474
Yes	233	10 (4.3)	223 (95.7)	NE (NE, NE)	112	1 (0.9)	111 (99.1)	NE (NE, NE)	3.7160 (0.4701, 29.3752) 0.2134	0.1822	
No	98	6 (6.1)	92 (93.9)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9953	0.1719	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9592
<65	289	15 (5.2)	274 (94.8)	NE (NE, NE)	126	2 (1.6)	124 (98.4)	NE (NE, NE)	2.7144 (0.6162, 11.9563) 0.1868	0.1693	
>=65	82	5 (6.1)	77 (93.9)	NE (NE, NE)	46	1 (2.2)	45 (97.8)	NE (NE, NE)	1.7387 (0.1939, 15.5872) 0.6211	0.6170	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9998
<75	357	20 (5.6)	337 (94.4)	NE (NE, NE)	163	3 (1.8)	160 (98.2)	NE (NE, NE)	2.3377 (0.6865, 7.9609) 0.1744	0.1619	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.7843
White	175	8 (4.6)	167 (95.4)	NE (NE, NE)	85	1 (1.2)	84 (98.8)	NE (NE, NE)	2.8479 (0.3505, 23.1378) 0.3275	0.3062	
Non-White	196	12 (6.1)	184 (93.9)	NE (NE, NE)	86	2 (2.3)	84 (97.7)	NE (NE, NE)	2.1518 (0.4750, 9.7484) 0.3202	0.3084	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.3870
Asia	147	9 (6.1)	138 (93.9)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (NE, NE)	3.2879 (0.4119, 26.2469) 0.2614	0.2337	
North America	58	1 (1.7)	57 (98.3)	NE (NE, NE)	28	1 (3.6)	27 (96.4)	NE (NE, NE)	0.3556 (0.0222, 5.6872) 0.4648	0.4449	
Europe + Israel	166	10 (6.0)	156 (94.0)	NE (NE, NE)	81	1 (1.2)	80 (98.8)	NE (NE, NE)	3.5759 (0.4511, 28.3488) 0.2277	0.1980	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.5780
0	199	10 (5.0)	189 (95.0)	NE (NE, NE)	95	1 (1.1)	94 (98.9)	NE (NE, NE)	3.6642 (0.4631, 28.9926) 0.2185	0.1879	
1	172	10 (5.8)	162 (94.2)	NE (NE, NE)	77	2 (2.6)	75 (97.4)	NE (NE, NE)	1.7583 (0.3780, 8.1796) 0.4718	0.4656	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.3315
0	60	6 (10.0)	54 (90.0)	NE (NE, NE)	31	2 (6.5)	29 (93.5)	NE (NE, NE)	1.1897 (0.2351, 6.0220) 0.8337	0.8335	
1	107	4 (3.7)	103 (96.3)	NE (NE, NE)	48	1 (2.1)	47 (97.9)	NE (NE, NE)	1.5814 (0.1752, 14.2764) 0.6831	0.6814	
2	114	5 (4.4)	109 (95.6)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	NE (NE, NE) 0.9960	0.2352	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	5 (5.6)	85 (94.4)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9954	0.1635	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.4773
PD	173	6 (3.5)	167 (96.5)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	2.1309 (0.2510, 18.0911)	0.4780	
PR	48	4 (8.3)	44 (91.7)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	NE (NE, NE)	0.1887	
SD	82	5 (6.1)	77 (93.9)	NE (NE, NE)	54	2 (3.7)	52 (96.3)	NE (NE, NE)	1.2208 (0.2299, 6.4818)	0.8138	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.3958
Yes	37	3 (8.1)	34 (91.9)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9965	0.3090	
No	334	17 (5.1)	317 (94.9)	NE (NE, NE)	159	3 (1.9)	156 (98.1)	NE (NE, NE)	2.0193 (0.5834, 6.9895) 0.2673	0.2577	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.5010
Yes	24	2 (8.3)	22 (91.7)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9973	0.4401	
No	347	18 (5.2)	329 (94.8)	NE (NE, NE)	165	3 (1.8)	162 (98.2)	NE (NE, NE)	2.1328 (0.6200, 7.3370) 0.2295	0.2188	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.2098
Normal Function	201	12 (6.0)	189 (94.0)	NE (NE, NE)	80	2 (2.5)	78 (97.5)	NE (NE, NE)	1.8566 (0.4087, 8.4340) 0.4230	0.4160	
Mild Impairment	123	6 (4.9)	117 (95.1)	NE (NE, NE)	65	0	65 (100)	NE (NE, NE)	NE (NE, NE) 0.9948	0.1108	
Moderate Impairment	41	1 (2.4)	40 (97.6)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	0.4103 (0.0248, 6.7870) 0.5338	0.5210	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.0407
Normal Function	170	8 (4.7)	162 (95.3)	NE (NE, NE)	88	3 (3.4)	85 (96.6)	NE (NE, NE)	0.9471 (0.2434, 3.6860) 0.9375	0.9378	
Mild Impairment	194	11 (5.7)	183 (94.3)	NE (NE, NE)	82	0	82 (100)	NE (NE, NE)	NE (NE, NE) 0.9933	0.0473	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.0880
Yes	331	17 (5.1)	314 (94.9)	NE (NE, NE)	146	1 (0.7)	145 (99.3)	NE (NE, NE)	6.2595 (0.8288, 47.2714) 0.0754	0.0418	
No	40	3 (7.5)	37 (92.5)	NE (NE, NE)	26	2 (7.7)	24 (92.3)	NE (NE, NE)	0.3833 (0.0483, 3.0416) 0.3642	0.3509	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.0073
Positive	329	15 (4.6)	314 (95.4)	NE (NE, NE)	152	0	152 (100)	NE (NE, NE)	NE (NE, NE) 0.9924	0.0246	
Negative	42	5 (11.9)	37 (88.1)	NE (NE, NE)	20	3 (15.0)	17 (85.0)	NE (NE, NE)	0.7022 (0.1656, 2.9781) 0.6315	0.6298	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: General disorders and administration site conditions; PT: Fatigue

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.0882
Positive	331	16 (4.8)	315 (95.2)	NE (NE, NE)	155	1 (0.6)	154 (99.4)	NE (NE, NE)	5.5558 (0.7295, 42.3116)	0.0627	
Negative	40	4 (10.0)	36 (90.0)	NE (NE, NE)	17	2 (11.8)	15 (88.2)	NE (NE, NE)	0.7312 (0.1309, 4.0841)	0.7203	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.9757
HER2 IHC 1+	214	22 (10.3)	192 (89.7)	NE (NE, NE)	100	4 (4.0)	96 (96.0)	NE (NE, NE)	2.0743 (0.7078, 6.0794) 0.1835	0.1745
HER2 IHC 2+/ISH Negative	157	17 (10.8)	140 (89.2)	NE (NE, NE)	72	3 (4.2)	69 (95.8)	NE (NE, NE)	2.2359 (0.6506, 7.6843) 0.2015	0.1903

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting									0.3575
1	220 (9.1)	200 (90.9)	NE (NE, NE)	94 (2.1)	92 (97.9)	NE (NE, NE)	3.5339 (0.8210, 15.2108) 0.0900	0.0706	
>=2	150 (12.7)	131 (87.3)	NE (NE, NE)	78 (6.4)	73 (93.6)	NE (NE, NE)	1.6987 (0.6289, 4.5887) 0.2960	0.2913	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											
Yes	233	24 (10.3)	209 (89.7)	NE (NE, NE)	112	3 (2.7)	109 (97.3)	NE (NE, NE)	3.0937 (0.9224, 10.3765) 0.0674	0.0542	0.3871
No	98	12 (12.2)	86 (87.8)	NE (NE, NE)	43	3 (7.0)	40 (93.0)	NE (NE, NE)	1.6058 (0.4524, 5.7003) 0.4637	0.4596	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3388
<65	289	27 (9.3)	262 (90.7)	NE (NE, NE)	126	3 (2.4)	123 (97.6)	NE (NE, NE)	3.3912 (1.0236, 11.2350) 0.0457	0.0338	
>=65	82	12 (14.6)	70 (85.4)	NE (NE, NE)	46	4 (8.7)	42 (91.3)	NE (NE, NE)	1.3305 (0.4219, 4.1956) 0.6261	0.6249	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.1534
<75	357	35 (9.8)	322 (90.2)	NE (NE, NE)	163	4 (2.5)	159 (97.5)	NE (NE, NE)	3.4207 (1.2101, 9.6700) 0.0204	0.0136	
>=75	14	4 (28.6)	10 (71.4)	14.7 (5.5, NE)	9	3 (33.3)	6 (66.7)	NE (0.5, NE)	0.7637 (0.1702, 3.4261) 0.7248	0.7240	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Race										0.3550
White	175	23 (13.1)	152 (86.9)	NE (NE, NE)	85	3 (3.5)	82 (96.5)	NE (NE, NE)	2.9432 (0.8758, 9.8908) 0.0809	0.0675
Non-White	196	16 (8.2)	180 (91.8)	NE (NE, NE)	86	4 (4.7)	82 (95.3)	NE (NE, NE)	1.5811 (0.5258, 4.7542) 0.4147	0.4113

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.0831
Asia	147	11 (7.5)	136 (92.5)	NE (NE, NE)	63	4 (6.3)	59 (93.7)	NE (NE, NE)	0.9690 (0.3051, 3.0772) 0.9574	0.9577	
North America	58	9 (15.5)	49 (84.5)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9940	0.0681	
Europe + Israel	166	19 (11.4)	147 (88.6)	NE (NE, NE)	81	3 (3.7)	78 (96.3)	NE (NE, NE)	2.6907 (0.7919, 9.1425) 0.1127	0.0991	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.5710
0	199	16 (8.0)	183 (92.0)	NE (NE, NE)	95	2 (2.1)	93 (97.9)	NE (NE, NE)	2.6594 (0.6046, 11.6971) 0.1956	0.1787	
1	172	23 (13.4)	149 (86.6)	NE (NE, NE)	77	5 (6.5)	72 (93.5)	NE (NE, NE)	1.9400 (0.7333, 5.1325) 0.1819	0.1748	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1849
0	60	3 (5.0)	57 (95.0)	NE (NE, NE)	31	3 (9.7)	28 (90.3)	NE (NE, NE)	0.3799 (0.0743, 1.9422)	0.2284	
1	107	6 (5.6)	101 (94.4)	NE (NE, NE)	48	1 (2.1)	47 (97.9)	NE (NE, NE)	2.1844 (0.2593, 18.3990)	0.4614	
2	114	23 (20.2)	91 (79.8)	NE (NE, NE)	50	2 (4.0)	48 (96.0)	NE (NE, NE)	4.5018 (1.0552, 19.2066)	0.0260	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

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Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 7 (7.8)	83 (92.2)	NE (NE, NE)	43 1 (2.3)	42 (97.7)	NE (NE, NE)	2.5495 (0.3073, 21.1501) 0.3859	0.3690	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.3940
PD	173	20 (11.6)	153 (88.4)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	7.7279 (1.0336, 57.7809)	0.0185	
PR	48	6 (12.5)	42 (87.5)	NE (NE, NE)	21	1 (4.8)	20 (95.2)	NE (NE, NE)	2.1374 (0.2554, 17.8899)	0.4731	
SD	82	9 (11.0)	73 (89.0)	NE (NE, NE)	54	3 (5.6)	51 (94.4)	NE (NE, NE)	1.4020 (0.3717, 5.2872)	0.6162	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.3693
Yes	37	3 (8.1)	34 (91.9)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9964	0.2978	
No	334	36 (10.8)	298 (89.2)	NE (NE, NE)	159	7 (4.4)	152 (95.6)	NE (NE, NE)	2.0065 (0.8870, 4.5388) 0.0945	0.0884	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Baseline CNS metastases										
Yes	24	2 (8.3)	22 (91.7)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	0.9973	0.4401
No	347	37 (10.7)	310 (89.3)	NE (NE, NE)	165	7 (4.2)	158 (95.8)	NE (NE, NE)	2.0550 (0.9101, 4.6401)	0.0769

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Renal function at baseline										0.0129
Normal Function	201	22 (10.9)	179 (89.1)	NE (NE, NE)	80	0	80 (100)	NE (NE, NE)	NE (NE, NE) 0.9907	0.0063
Mild Impairment	123	11 (8.9)	112 (91.1)	NE (NE, NE)	65	5 (7.7)	60 (92.3)	NE (NE, NE)	0.9261 (0.3187, 2.6910) 0.8879	0.8870
Moderate Impairment	41	6 (14.6)	35 (85.4)	NE (14.7, NE)	23	2 (8.7)	21 (91.3)	NE (NE, NE)	1.6002 (0.3222, 7.9481) 0.5654	0.5615

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Hepatic function at baseline											
Normal Function	170	18 (10.6)	152 (89.4)	NE (NE, NE)	88	3 (3.4)	85 (96.6)	NE (NE, NE)	2.7433 (0.8035, 9.3660) 0.1072	0.0933	0.6557
Mild Impairment	194	21 (10.8)	173 (89.2)	NE (NE, NE)	82	4 (4.9)	78 (95.1)	NE (NE, NE)	1.7408 (0.5912, 5.1263) 0.3144	0.3090	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.2765
Yes	331	38 (11.5)	293 (88.5)	NE (NE, NE)	146	6 (4.1)	140 (95.9)	NE (NE, NE)	2.3682 (0.9964, 5.6282) 0.0509	0.0444	
No	40	1 (2.5)	39 (97.5)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	0.6583 (0.0412, 10.5249) 0.7675	0.7658	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Hormon receptor status (IXRS)										0.6056
Positive	329	36 (10.9)	293 (89.1)	NE (NE, NE)	152	6 (3.9)	146 (96.1)	NE (NE, NE)	2.3412 (0.9814, 5.5853) 0.0552	0.0484
Negative	42	3 (7.1)	39 (92.9)	NE (NE, NE)	20	1 (5.0)	19 (95.0)	NE (4.9, NE)	0.8875 (0.0863, 9.1272) 0.9200	0.9200

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.5274
Positive	331	36 (10.9)	295 (89.1)	NE (NE, NE)	155	6 (3.9)	149 (96.1)	NE (NE, NE)	2.3779 (0.9967, 5.6733)	0.0442	
Negative	40	3 (7.5)	37 (92.5)	NE (NE, NE)	17	1 (5.9)	16 (94.1)	NE (4.9, NE)	0.7005 (0.0652, 7.5249)	0.7680	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
HER2 status										
HER2 IHC 1+	214	8 (3.7)	206 (96.3)	NE (NE, NE)	100	0	100 (100)	NE (NE, NE) 0.9938	0.0588	0.9998
HER2 IHC 2+/ISH Negative	157	9 (5.7)	148 (94.3)	NE (NE, NE)	72	0	72 (100)	NE (NE, NE) 0.9936	0.0528	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting									0.9997
1	220 (3.2)	213 (96.8)	NE (NE, NE)	94	0	94 (100) (NE, NE)	NE (NE, NE) 0.9945	0.1091	
>=2	150 (6.7)	140 (93.3)	NE (NE, NE)	78	0	78 (100) (NE, NE)	NE (NE, NE) 0.9928	0.0230	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.9998
Yes	233	9 (3.9)	224 (96.1)	NE (NE, NE)	112	0	112 (100)	NE (NE, NE)	NE (NE, NE) 0.9934	0.0411	
No	98	6 (6.1)	92 (93.9)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9948	0.1179	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9999
<65	289	14 (4.8)	275 (95.2)	NE (NE, NE)	126	0	126 (100)	NE (NE, NE)	NE (NE, NE) 0.9920	0.0171	
>=65	82	3 (3.7)	79 (96.3)	NE (NE, NE)	46	0	46 (100)	NE (NE, NE)	NE (NE, NE) 0.9961	0.2292	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											NE
<75	357	15 (4.2)	342 (95.8)	NE (NE, NE)	163	0	163 (100)	NE (NE, NE)	NE (NE, NE) 0.9916	0.0111	
>=75	14	2 (14.3)	12 (85.7)	NE (5.5, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9979	0.2855	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.9999
White	175	7 (4.0)	168 (96.0)	NE (NE, NE)	85	0	85 (100)	NE (NE, NE)	NE (NE, NE) 0.9943	0.0793	
Non-White	196	10 (5.1)	186 (94.9)	NE (NE, NE)	86	0	86 (100)	NE (NE, NE)	NE (NE, NE) 0.9932	0.0418	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Region										1.0000
Asia	147	8 (5.4)	139 (94.6)	NE (NE, NE)	63	0	63 (100)	NE (NE, NE)	NE (NE, NE) 0.9940	0.0778
North America	58	3 (5.2)	55 (94.8)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9961	0.2243
Europe + Israel	166	6 (3.6)	160 (96.4)	NE (NE, NE)	81	0	81 (100)	NE (NE, NE)	NE (NE, NE) 0.9947	0.1040

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.12.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											
0	199	6 (3.0)	193 (97.0)	NE (NE, NE)	95	0	95 (100)	NE (NE, NE)	NE (NE, NE) 0.9949	0.1257	0.9997
1	172	11 (6.4)	161 (93.6)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE) 0.9927	0.0264	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											1.0000
0	60	1 (1.7)	59 (98.3)	NE (NE, NE)	31	0	31 (100)	NE (NE, NE)	NE (NE, NE) 0.9977	0.4723	
1	107	1 (0.9)	106 (99.1)	NE (NE, NE)	48	0	48 (100)	NE (NE, NE)	NE (NE, NE) 0.9978	0.5040	
2	114	12 (10.5)	102 (89.5)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	NE (NE, NE) 0.9926	0.0264	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 3 (3.3)	87 (96.7)	NE (NE, NE)	43 0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9963	0.2673	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy									NE
PD	173	7 (4.0)	166 (96.0)	77	0	77 (100) (NE, NE)	NE (NE, NE) 0.9945	0.1016	
PR	48	5 (10.4)	43 (89.6)	21	0	21 (100) (NE, NE)	NE (NE, NE) 0.9952	0.1566	
SD	82	2 (2.4)	80 (97.6)	54	0	54 (100) (NE, NE)	NE (NE, NE) 0.9966	0.2631	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.9999
Yes	37	1 (2.7)	36 (97.3)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9980	0.5533	
No	334	16 (4.8)	318 (95.2)	NE (NE, NE)	159	0	159 (100)	NE (NE, NE)	NE (NE, NE) 0.9913	0.0080	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											1.0000
Yes	24	1 (4.2)	23 (95.8)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9981	0.5892	
No	347	16 (4.6)	331 (95.4)	NE (NE, NE)	165	0	165 (100)	NE (NE, NE)	NE (NE, NE) 0.9913	0.0083	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
Renal function at baseline										1.0000
Normal Function	201	11 (5.5)	190 (94.5)	NE (NE, NE)	80	0	80 (100)	NE (NE, NE)	NE (NE, NE) 0.9930	0.0389
Mild Impairment	123	4 (3.3)	119 (96.7)	NE (NE, NE)	65	0	65 (100)	NE (NE, NE)	NE (NE, NE) 0.9958	0.2010
Moderate Impairment	41	2 (4.9)	39 (95.1)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9967	0.2848

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Hepatic function at baseline										
Normal Function	170	9 (5.3)	161 (94.7)	NE (NE, NE)	88	0	88 (100) (NE, NE)	NE (NE, NE) 0.9933	0.0351	0.9999
Mild Impairment	194	8 (4.1)	186 (95.9)	NE (NE, NE)	82	0	82 (100) (NE, NE)	NE (NE, NE) 0.9941	0.0842	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.9995
Yes	331	17 (5.1)	314 (94.9)	NE (NE, NE)	146	0	146 (100)	NE (NE, NE)	NE (NE, NE) 0.9912	0.0081	
No	40	0	40 (100)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											1.0000
Positive	329	15 (4.6)	314 (95.4)	NE (NE, NE)	152	0	152 (100)	NE (NE, NE)	NE (NE, NE) 0.9916	0.0105	
Negative	42	2 (4.8)	40 (95.2)	NE (NE, NE)	20	0	20 (100)	NE (NE, NE)	NE (NE, NE) 0.9973	0.4254	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.12.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Gastrointestinal disorders; PT: Nausea

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											1.0000
Positive	331	15 (4.5)	316 (95.5)	NE (NE, NE)	155	0	155 (100)	NE (NE, NE)	NE (NE, NE) 0.9915	0.0098	
Negative	40	2 (5.0)	38 (95.0)	NE (NE, NE)	17	0	17 (100)	NE (NE, NE)	NE (NE, NE) 0.9974	0.4608	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.12.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]
HER2 status										0.7774
HER2 IHC 1+	214	18 (8.4)	196 (91.6)	NE (NE, NE)	100	3 (3.0)	97 (97.0)	NE (NE, NE)	1.6770 (0.4873, 5.7715) 0.4123	0.4075
HER2 IHC 2+/ISH Negative	157	14 (8.9)	143 (91.1)	NE (NE, NE)	72	3 (4.2)	69 (95.8)	NE (NE, NE)	1.3923 (0.3935, 4.9261) 0.6077	0.6059

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.7415
1	220	14 (6.4)	206 (93.6)	NE (NE, NE)	94	3 (3.2)	91 (96.8)	NE (NE, NE)	1.2187 (0.3447, 4.3084) 0.7588	0.7596	
>=2	150	18 (12.0)	132 (88.0)	NE (NE, NE)	78	3 (3.8)	75 (96.2)	NE (NE, NE)	1.9243 (0.5576, 6.6407) 0.3003	0.2923	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.1152
Yes	233	17 (7.3)	216 (92.7)	NE (NE, NE)	112	1 (0.9)	111 (99.1)	NE (NE, NE)	5.0042 (0.6570, 38.1182) 0.1201	0.0849	
No	98	8 (8.2)	90 (91.8)	NE (NE, NE)	43	3 (7.0)	40 (93.0)	NE (NE, NE)	0.7665 (0.2024, 2.9021) 0.6954	0.6946	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9831
<65	289	24 (8.3)	265 (91.7)	NE (NE, NE)	126	4 (3.2)	122 (96.8)	NE (NE, NE)	1.7140 (0.5881, 4.9955) 0.3235	0.3182	
>=65	82	8 (9.8)	74 (90.2)	NE (NE, NE)	46	2 (4.3)	44 (95.7)	NE (NE, NE)	1.2613 (0.2630, 6.0483) 0.7716	0.7711	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.7535
<75	357	30 (8.4)	327 (91.6)	NE (NE, NE)	163	5 (3.1)	158 (96.9)	NE (NE, NE)	1.7332 (0.6649, 4.5184) 0.2606	0.2550	
>=75	14	2 (14.3)	12 (85.7)	NE (5.5, NE)	9	1 (11.1)	8 (88.9)	NE (4.7, NE)	0.9301 (0.0841, 10.2866) 0.9529	0.9528	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.2793
White	175	18 (10.3)	157 (89.7)	NE (NE, NE)	85	2 (2.4)	83 (97.6)	NE (NE, NE)	2.8186 (0.6476, 12.2671) 0.1673	0.1493	
Non-White	196	14 (7.1)	182 (92.9)	NE (NE, NE)	86	4 (4.7)	82 (95.3)	NE (NE, NE)	0.9371 (0.3026, 2.9025) 0.9103	0.9103	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.0441
Asia	147	8 (5.4)	139 (94.6)	NE (NE, NE)	63	4 (6.3)	59 (93.7)	NE (NE, NE)	0.4842 (0.1429, 1.6414) 0.2443	0.2347	
North America	58	9 (15.5)	49 (84.5)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9944	0.1112	
Europe + Israel	166	15 (9.0)	151 (91.0)	NE (NE, NE)	81	2 (2.5)	79 (97.5)	NE (NE, NE)	2.6025 (0.5879, 11.5206) 0.2076	0.1913	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
ECOG PS											
0	199	11 (5.5)	188 (94.5)	NE (NE, NE)	95	3 (3.2)	92 (96.8)	NE (NE, NE)	0.9670 (0.2647, 3.5324) 0.9595	0.9599	0.4801
1	172	21 (12.2)	151 (87.8)	NE (NE, NE)	77	3 (3.9)	74 (96.1)	NE (NE, NE)	2.1207 (0.6244, 7.2026) 0.2282	0.2179	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.0767
0	60	9 (15.0)	51 (85.0)	NE (NE, NE)	31	3 (9.7)	28 (90.3)	NE (4.7, NE)	0.8457 (0.2228, 3.2093) 0.8054	0.8052	
1	107	7 (6.5)	100 (93.5)	NE (NE, NE)	48	1 (2.1)	47 (97.9)	NE (NE, NE)	2.7840 (0.3411, 22.7207) 0.3391	0.3183	
2	114	13 (11.4)	101 (88.6)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	NE (NE, NE) 0.9940	0.0959	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.12.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 3 (3.3)	87 (96.7)	NE (NE, NE)	43 2 (4.7)	41 (95.3)	NE (NE, NE)	0.3647 (0.0572, 2.3252) 0.2859	0.2686	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.2168
PD	173	15 (8.7)	158 (91.3)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	3.8294 (0.4983, 29.4265)	0.1654	
PR	48	3 (6.3)	45 (93.8)	NE (NE, NE)	21	1 (4.8)	20 (95.2)	NE (NE, NE)	0.1969 (0.0665, 7.2484)	0.7596	
SD	82	4 (4.9)	78 (95.1)	NE (NE, NE)	54	3 (5.6)	51 (94.4)	NE (NE, NE)	0.6944 (0.1424, 2.9168)	0.5656	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.1616
Yes	37	1 (2.7)	36 (97.3)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	0.2265 (0.0134, 3.8135)	0.2626	
No	334	31 (9.3)	303 (90.7)	NE (NE, NE)	159	5 (3.1)	154 (96.9)	NE (NE, NE)	1.8486 (0.7114, 4.8036)	0.2006	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0371
Yes	24	0	24 (100)	NE (NE, NE)	7	1 (14.3)	6 (85.7)	NE (0.8, NE)	0.0000 (0.0000, ) 0.9982	0.0699	
No	347	32 (9.2)	315 (90.8)	NE (NE, NE)	165	5 (3.0)	160 (97.0)	NE (NE, NE)	1.8642 (0.7188, 4.8344) 0.2002	0.1934	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]	
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]		Unstratified log-rank p-value [c]
Renal function at baseline										0.2774
Normal Function	201	17 (8.5)	184 (91.5)	NE (NE, NE)	80	3 (3.8)	77 (96.3)	NE (NE, NE)	1.3573 (0.3906, 4.7165) 0.6307	0.6297
Mild Impairment	123	10 (8.1)	113 (91.9)	NE (NE, NE)	65	3 (4.6)	62 (95.4)	NE (NE, NE)	1.0880 (0.2924, 4.0484) 0.8999	0.8999
Moderate Impairment	41	4 (9.8)	37 (90.2)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9957	0.1885

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.6291
Normal Function	170	15 (8.8)	155 (91.2)	NE (NE, NE)	88	4 (4.5)	84 (95.5)	NE (NE, NE)	0.9517 (0.3118, 2.9053) 0.9307	0.9301	
Mild Impairment	194	15 (7.7)	179 (92.3)	NE (NE, NE)	82	2 (2.4)	80 (97.6)	NE (NE, NE)	2.3422 (0.5312, 10.3275) 0.2609	0.2469	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.8616
Yes	331	28 (8.5)	303 (91.5)	NE (NE, NE)	146	5 (3.4)	141 (96.6)	NE (NE, NE)	1.6564 (0.6335, 4.3306) 0.3034	0.2988	
No	40	4 (10.0)	36 (90.0)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	0.8814 (0.0943, 8.2396) 0.9119	0.9118	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.1400
Positive	329	25 (7.6)	304 (92.4)	NE (NE, NE)	152	3 (2.0)	149 (98.0)	NE (NE, NE)	2.2848 (0.6832, 7.6406) 0.1797	0.1680	
Negative	42	7 (16.7)	35 (83.3)	NE (NE, NE)	20	3 (15.0)	17 (85.0)	NE (4.7, NE)	0.7932 (0.1955, 3.2182) 0.7457	0.7452	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Infections and infestations; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.2724
Positive	331	26 (7.9)	305 (92.1)	NE (NE, NE)	155	4 (2.6)	151 (97.4)	NE (NE, NE)	1.8725 (0.6468, 5.4213) 0.2475	0.2402	
Negative	40	6 (15.0)	34 (85.0)	NE (NE, NE)	17	2 (11.8)	15 (88.2)	NE (4.7, NE)	0.7646 (0.1437, 4.0683) 0.7530	0.7524	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.7968
HER2 IHC 1+	214	17 (7.9)	197 (92.1)	NE (NE, NE)	100	4 (4.0)	96 (96.0)	NE (NE, NE)	1.4884 (0.4930, 4.4937) 0.4806	0.4783	
HER2 IHC 2+/ISH Negative	157	14 (8.9)	143 (91.1)	NE (NE, NE)	72	4 (5.6)	68 (94.4)	NE (NE, NE)	1.2864 (0.4192, 3.9479) 0.6598	0.6602	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.3545
1	220	15 (6.8)	205 (93.2)	NE (NE, NE)	94	5 (5.3)	89 (94.7)	NE (NE, NE)	0.9233 (0.3296, 2.5863) 0.8793	0.8778	
>=2	150	16 (10.7)	134 (89.3)	NE (NE, NE)	78	3 (3.8)	75 (96.2)	NE (NE, NE)	2.3082 (0.6663, 7.9961) 0.1870	0.1749	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.0865
Yes	233	22 (9.4)	211 (90.6)	NE (NE, NE)	112	6 (5.4)	106 (94.6)	NE (NE, NE)	1.3563 (0.5430, 3.3878) 0.5141	0.5135	
No	98	7 (7.1)	91 (92.9)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9948	0.1390	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9698
<65	289	22 (7.6)	267 (92.4)	NE (NE, NE)	126	5 (4.0)	121 (96.0)	NE (NE, NE)	1.5507 (0.5825, 4.1286) 0.3798	0.3756	
>=65	82	9 (11.0)	73 (89.0)	NE (NE, NE)	46	3 (6.5)	43 (93.5)	NE (NE, NE)	1.2435 (0.3303, 4.6812) 0.7472	0.7479	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.3753
<75	357	30 (8.4)	327 (91.6)	NE (NE, NE)	163	8 (4.9)	155 (95.1)	NE (NE, NE)	1.3005 (0.5896, 2.8686) 0.5150	0.5143	
>=75	14	1 (7.1)	13 (92.9)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) 0.9985	0.4142	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.3195
White	175	17 (9.7)	158 (90.3)	NE (NE, NE)	85	6 (7.1)	79 (92.9)	NE (NE, NE)	1.0169 (0.3947, 2.6204) 0.9723	0.9730	
Non-White	196	14 (7.1)	182 (92.9)	NE (NE, NE)	86	2 (2.3)	84 (97.7)	NE (NE, NE)	2.4710 (0.5559, 10.9829) 0.2346	0.2196	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.3614
Asia	147	12 (8.2)	135 (91.8)	NE (NE, NE)	63	2 (3.2)	61 (96.8)	NE (NE, NE)	2.0739 (0.4588, 9.3735) 0.3433	0.3337	
North America	58	3 (5.2)	55 (94.8)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9962	0.2467	
Europe + Israel	166	16 (9.6)	150 (90.4)	NE (NE, NE)	81	6 (7.4)	75 (92.6)	NE (NE, NE)	0.9622 (0.3707, 2.4971) 0.9368	0.9355	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.3532
0	199	13 (6.5)	186 (93.5)	NE (NE, NE)	95	2 (2.1)	93 (97.9)	NE (NE, NE)	2.5414 (0.5692, 11.3476) 0.2218	0.2059	
1	172	18 (10.5)	154 (89.5)	NE (NE, NE)	77	6 (7.8)	71 (92.2)	NE (NE, NE)	0.9852 (0.3835, 2.5307) 0.9753	0.9749	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1037
0	60	5 (8.3)	55 (91.7)	NE (NE, NE)	31	2 (6.5)	29 (93.5)	NE (NE, NE)	1.0178 (0.1902, 5.4470) 0.9836	0.9835	
1	107	10 (9.3)	97 (90.7)	NE (NE, NE)	48	3 (6.3)	45 (93.8)	NE (NE, NE)	1.2432 (0.3392, 4.5566) 0.7425	0.7436	
2	114	11 (9.6)	103 (90.4)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	NE (NE, NE) 0.9932	0.0443	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	5 (5.6)	85 (94.4)	NE (NE, NE)	43	3 (7.0)	40 (93.0)	NE (NE, NE)	0.5271 (0.1199, 2.3172) 0.3966	0.3898	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.4183
PD	173	11 (6.4)	162 (93.6)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	3.7915 (0.4846, 29.6667) 0.2042	0.1726	
PR	48	5 (10.4)	43 (89.6)	NE (NE, NE)	21	1 (4.8)	20 (95.2)	NE (NE, NE)	1.5911 (0.1822, 13.8913) 0.6744	0.6717	
SD	82	9 (11.0)	73 (89.0)	NE (NE, NE)	54	5 (9.3)	49 (90.7)	NE (NE, NE)	0.9026 (0.2966, 2.7467) 0.8567	0.8571	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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DE.T.4.12.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.0429
Yes	37	0	37 (100)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	0.0000 (0.0000, ) 0.9980	0.0916	
No	334	31 (9.3)	303 (90.7)	NE (NE, NE)	159	7 (4.4)	152 (95.6)	NE (NE, NE)	1.6479 (0.7196, 3.7735) 0.2374	0.2331	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.0381
Yes	24	0	24 (100)	NE (NE, NE)	7	1 (14.3)	6 (85.7)	NE (0.1, NE)	0.0000 (0.0000, ) 0.9983	0.0641	
No	347	31 (8.9)	316 (91.1)	NE (NE, NE)	165	7 (4.2)	158 (95.8)	NE (NE, NE)	1.6285 (0.7109, 3.7306) 0.2489	0.2448	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.9812
Normal Function	201	13 (6.5)	188 (93.5)	NE (NE, NE)	80	3 (3.8)	77 (96.3)	NE (NE, NE)	1.4825 (0.4200, 5.2329) 0.5406	0.5375	
Mild Impairment	123	12 (9.8)	111 (90.2)	NE (NE, NE)	65	3 (4.6)	62 (95.4)	NE (NE, NE)	1.3108 (0.3562, 4.8238) 0.6839	0.6830	
Moderate Impairment	41	6 (14.6)	35 (85.4)	NE (NE, NE)	23	2 (8.7)	21 (91.3)	NE (NE, NE)	1.5080 (0.3035, 7.4914) 0.6155	0.6070	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.7277
Normal Function	170	12 (7.1)	158 (92.9)	NE (NE, NE)	88	3 (3.4)	85 (96.6)	NE (NE, NE)	1.3023 (0.3571, 4.7490) 0.6891	0.6870	
Mild Impairment	194	18 (9.3)	176 (90.7)	NE (NE, NE)	82	5 (6.1)	77 (93.9)	NE (NE, NE)	1.2969 (0.4788, 3.5131) 0.6091	0.6095	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.2111
Yes	331	29 (8.8)	302 (91.2)	NE (NE, NE)	146	6 (4.1)	140 (95.9)	NE (NE, NE)	1.6984 (0.7002, 4.1194) 0.2413	0.2362	
No	40	2 (5.0)	38 (95.0)	NE (NE, NE)	26	2 (7.7)	24 (92.3)	NE (NE, NE)	0.3999 (0.0465, 3.4374) 0.4037	0.3903	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.1628
Positive	329	29 (8.8)	300 (91.2)	NE (NE, NE)	152	6 (3.9)	146 (96.1)	NE (NE, NE)	1.6928 (0.6967, 4.1131) 0.2452	0.2402	
Negative	42	2 (4.8)	40 (95.2)	NE (NE, NE)	20	2 (10.0)	18 (90.0)	NE (NE, NE)	0.4786 (0.0674, 3.3978) 0.4612	0.4510	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.1223
Positive	331	29 (8.8)	302 (91.2)	NE (NE, NE)	155	6 (3.9)	149 (96.1)	NE (NE, NE)	1.7204 (0.7080, 4.1807) 0.2310	0.2258	
Negative	40	2 (5.0)	38 (95.0)	NE (NE, NE)	17	2 (11.8)	15 (88.2)	NE (NE, NE)	0.4259 (0.0600, 3.0237) 0.3933	0.3789	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.9980
HER2 IHC 1+	214	5 (2.3)	209 (97.7)	NE (NE, NE)	100	1 (1.0)	99 (99.0)	NE (NE, NE)	1.8378 (0.2111, 15.9970) 0.5815	0.5758	
HER2 IHC 2+/ISH Negative	157	5 (3.2)	152 (96.8)	NE (NE, NE)	72	1 (1.4)	71 (98.6)	NE (NE, NE)	1.7172 (0.1971, 14.9615) 0.6244	0.6208	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.9267
1	220	5 (2.3)	215 (97.7)	NE (NE, NE)	94	1 (1.1)	93 (98.9)	NE (NE, NE)	1.6115 (0.1863, 13.9374) 0.6647	0.6621	
>=2	150	5 (3.3)	145 (96.7)	NE (NE, NE)	78	1 (1.3)	77 (98.7)	NE (NE, NE)	2.1130 (0.2413, 18.5012) 0.4992	0.4895	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.6584
Yes	233	9 (3.9)	224 (96.1)	NE (NE, NE)	112	1 (0.9)	111 (99.1)	NE (NE, NE)	3.1130 (0.3887, 24.9315) 0.2847	0.2598	
No	98	1 (1.0)	97 (99.0)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9978	0.5055	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
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DE.T.4.12.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.2948
<65	289	8 (2.8)	281 (97.2)	NE (NE, NE)	126	2 (1.6)	124 (98.4)	NE (NE, NE)	1.4014 (0.2939, 6.6838) 0.6720	0.6706	
>=65	82	2 (2.4)	80 (97.6)	NE (NE, NE)	46	0	46 (100)	NE (NE, NE)	NE (NE, NE) 0.9971	0.3861	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.9999
<75	357	10 (2.8)	347 (97.2)	NE (NE, NE)	163	2 (1.2)	161 (98.8)	NE (NE, NE)	1.7409 (0.3764, 8.0515) 0.4780	0.4726	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.2713
White	175	7 (4.0)	168 (96.0)	NE (NE, NE)	85	2 (2.4)	83 (97.6)	NE (NE, NE)	1.3182 (0.2704, 6.4268) 0.7325	0.7322	
Non-White	196	3 (1.5)	193 (98.5)	NE (NE, NE)	86	0	86 (100)	NE (NE, NE)	NE (NE, NE) 0.9966	0.3156	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.3275
Asia	147	3 (2.0)	144 (98.0)	NE (NE, NE)	63	0	63 (100)	NE (NE, NE)	NE (NE, NE) 0.9966	0.3257	
North America	58	2 (3.4)	56 (96.6)	NE (NE, NE)	28	0	28 (100)	NE (NE, NE)	NE (NE, NE) 0.9970	0.3586	
Europe + Israel	166	5 (3.0)	161 (97.0)	NE (NE, NE)	81	2 (2.5)	79 (97.5)	NE (NE, NE)	0.9401 (0.1789, 4.9406) 0.9418	0.9407	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.1130
0	199	5 (2.5)	194 (97.5)	NE (NE, NE)	95	2 (2.1)	93 (97.9)	NE (NE, NE)	0.8892 (0.1696, 4.6619) 0.8895	0.8894	
1	172	5 (2.9)	167 (97.1)	NE (NE, NE)	77	0	77 (100)	NE (NE, NE)	NE (NE, NE) 0.9955	0.1786	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.1555
0	60	1 (1.7)	59 (98.3)	NE (NE, NE)	31	1 (3.2)	30 (96.8)	NE (NE, NE)	0.4030 (0.0247, 6.5648) 0.5232	0.5093	
1	107	3 (2.8)	104 (97.2)	NE (NE, NE)	48	0	48 (100)	NE (NE, NE)	NE (NE, NE) 0.9964	0.2896	
2	114	5 (4.4)	109 (95.6)	NE (NE, NE)	50	0	50 (100)	NE (NE, NE)	NE (NE, NE) 0.9957	0.2088	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	1 (1.1)	89 (98.9)	NE (NE, NE)	43	1 (2.3)	42 (97.7)	NE (NE, NE)	0.4225 (0.0263, 6.7906) 0.5432	0.5307	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.7831
PD	173	3 (1.7)	170 (98.3)	NE (NE, NE)	77	1 (1.3)	76 (98.7)	NE (NE, NE)	1.0572 (0.1090, 10.2520)	0.9628	
PR	48	1 (2.1)	47 (97.9)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	0.9617 (NE, NE)	0.7664	
SD	82	3 (3.7)	79 (96.3)	NE (NE, NE)	54	1 (1.9)	53 (98.1)	NE (NE, NE)	1.8561 (0.1928, 17.8662)	0.5865	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.9999
Yes	37	0	37 (100)	NE (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE)		
No	334	10 (3.0)	324 (97.0)	NE (NE, NE)	159	2 (1.3)	157 (98.7)	NE (NE, NE)	1.8517 (0.4008, 8.5538)	0.4231	0.4301

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.9999
Yes	24	0	24 (100)	NE (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE)		
No	347	10 (2.9)	337 (97.1)	NE (NE, NE)	165	2 (1.2)	163 (98.8)	NE (NE, NE)	1.8271 (0.3953, 8.4452) 0.4403	0.4337	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.4128
Normal Function	201	7 (3.5)	194 (96.5)	NE (NE, NE)	80	2 (2.5)	78 (97.5)	NE (NE, NE)	1.1199 (0.2290, 5.4760) 0.8888	0.8893	
Mild Impairment	123	1 (0.8)	122 (99.2)	NE (NE, NE)	65	0	65 (100)	NE (NE, NE)	NE (NE, NE) 0.9979	0.5340	
Moderate Impairment	41	2 (4.9)	39 (95.1)	NE (NE, NE)	23	0	23 (100)	NE (NE, NE)	NE (NE, NE) 0.9968	0.3222	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1437
Normal Function	170	4 (2.4)	166 (97.6)	NE (NE, NE)	88	0	88 (100)	NE (NE, NE)	NE (NE, NE) 0.9962	0.2746	
Mild Impairment	194	6 (3.1)	188 (96.9)	NE (NE, NE)	82	2 (2.4)	80 (97.6)	NE (NE, NE)	1.0953 (0.2202, 5.4476) 0.9114	0.9114	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.0506
Yes	331	10 (3.0)	321 (97.0)	NE (NE, NE)	146	1 (0.7)	145 (99.3)	NE (NE, NE)	3.4527 (0.4388, 27.1689) 0.2391	0.2101	
No	40	0	40 (100)	NE (NE, NE)	26	1 (3.8)	25 (96.2)	NE (NE, NE)	0.0000 (0.0000, ) 0.9975	0.2207	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Hormon receptor status (XRS)											0.0427
Positive	329	10 (3.0)	319 (97.0)	NE (NE, NE)	152	1 (0.7)	151 (99.3)	NE (NE, NE)	3.5520 (0.4507, 27.9914)	0.1991	
Negative	42	0	42 (100)	NE (NE, NE)	20	1 (5.0)	19 (95.0)	NE (NE, NE)	0.2288 (0.0000, ) 0.9977	0.1522	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Metabolism and nutrition disorders; PT: Hypokalaemia

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.0359
Positive	331	10 (3.0)	321 (97.0)	NE (NE, NE)	155	1 (0.6)	154 (99.4)	NE (NE, NE)	3.6094 (0.4580, 28.4474)	0.1928	
Negative	40	0	40 (100)	NE (NE, NE)	17	1 (5.9)	16 (94.1)	NE (NE, NE)	0.2230 (0.0000, ) 0.9978	0.1299	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.4035
HER2 IHC 1+	214	9 (4.2)	205 (95.8)	NE (NE, NE)	100	5 (5.0)	95 (95.0)	NE (NE, NE)	0.4755 (0.1523, 1.4849) 0.2007	0.1916	
HER2 IHC 2+/ISH Negative	157	11 (7.0)	146 (93.0)	NE (24.4, NE)	72	3 (4.2)	69 (95.8)	NE (NE, NE)	0.9652 (0.2608, 3.5726) 0.9577	0.9573	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of prior lines of chemotherapy in a metastatic setting											0.4687
1	220	7 (3.2)	213 (96.8)	NE (24.4, NE)	94	4 (4.3)	90 (95.7)	NE (NE, NE)	0.4230 (0.1167, 1.5331) 0.1903	0.1782	
>=2	150	13 (8.7)	137 (91.3)	NE (NE, NE)	78	4 (5.1)	74 (94.9)	NE (NE, NE)	0.9084 (0.2863, 2.8816) 0.8704	0.8696	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.1559
Yes	233	13 (5.6)	220 (94.4)	NE (24.4, NE)	112	6 (5.4)	106 (94.6)	NE (NE, NE)	0.5170 (0.1883, 1.4193) 0.2004	0.1930	
No	98	3 (3.1)	95 (96.9)	NE (NE, NE)	43	0	43 (100)	NE (NE, NE)	NE (NE, NE) 0.9971	0.3960	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Age											0.0797
<65	289	19 (6.6)	270 (93.4)	NE (24.4, NE)	126	5 (4.0)	121 (96.0)	NE (NE, NE)	0.9327 (0.3398, 2.5606) 0.8925	0.8922	
>=65	82	1 (1.2)	81 (98.8)	NE (NE, NE)	46	3 (6.5)	43 (93.5)	NE (NE, NE)	0.1188 (0.0119, 1.1818) 0.0691	0.0321	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											0.9998
<75	357	20 (5.6)	337 (94.4)	NE (24.4, NE)	163	8 (4.9)	155 (95.1)	NE (NE, NE)	0.6410 (0.2747, 1.4959) 0.3037	0.3006	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.7259
White	175	16 (9.1)	159 (90.9)	24.4 (24.4, NE)	85	6 (7.1)	79 (92.9)	NE (NE, NE)	0.7229 (0.2745, 1.9039) 0.5114	0.5099	
Non-White	196	4 (2.0)	192 (98.0)	NE (NE, NE)	86	2 (2.3)	84 (97.7)	NE (NE, NE)	0.4891 (0.0846, 2.8258) 0.4242	0.4149	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.2973
Asia	147	3 (2.0)	144 (98.0)	NE (NE, NE)	63	1 (1.6)	62 (98.4)	NE (NE, NE)	0.6639 (0.0639, 6.8992) 0.7317	0.7303	
North America	58	8 (13.8)	50 (86.2)	NE (NE, NE)	28	1 (3.6)	27 (96.4)	NE (NE, NE)	2.1748 (0.2640, 17.9161) 0.4702	0.4593	
Europe + Israel	166	9 (5.4)	157 (94.6)	24.4 (24.4, NE)	81	6 (7.4)	75 (92.6)	NE (NE, NE)	0.4253 (0.1442, 1.2537) 0.1211	0.1109	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											0.2797
0	199	4 (2.0)	195 (98.0)	NE (24.4, NE)	95	3 (3.2)	92 (96.8)	NE (NE, NE)	0.2990 (0.0598, 1.4952) 0.1415	0.1192	
1	172	16 (9.3)	156 (90.7)	NE (NE, NE)	77	5 (6.5)	72 (93.5)	NE (NE, NE)	0.8575 (0.3050, 2.4105) 0.7706	0.7709	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.3633
0	60	5 (8.3)	55 (91.7)	NE (18.1, NE)	31	2 (6.5)	29 (93.5)	NE (NE, NE)	0.6869 (0.1237, 3.8142) 0.6677	0.6621	
1	107	5 (4.7)	102 (95.3)	NE (NE, NE)	48	3 (6.3)	45 (93.8)	NE (NE, NE)	0.5431 (0.1287, 2.2918) 0.4060	0.3989	
2	114	8 (7.0)	106 (93.0)	NE (NE, NE)	50	1 (2.0)	49 (98.0)	NE (NE, NE)	1.8430 (0.2227, 15.2547) 0.5707	0.5650	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90	2 (2.2)	88 (97.8)	NE (24.4, NE)	43	2 (4.7)	41 (95.3)	NE (NE, NE)	0.2245 (0.0203, 2.4792) 0.2228	0.1818	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Best Response to last prior cancer systemic therapy											0.9555
PD	173	12 (6.9)	161 (93.1)	NE (24.4, NE)	77	5 (6.5)	72 (93.5)	NE (NE, NE)	0.5349 (0.1771, 1.6151) 0.2671	0.2599	
PR	48	2 (4.2)	46 (95.8)	NE (NE, NE)	21	1 (4.8)	20 (95.2)	NE (NE, NE)	0.6718 (0.0597, 7.5585) 0.7474	0.7460	
SD	82	1 (1.2)	81 (98.8)	NE (NE, NE)	54	1 (1.9)	53 (98.1)	NE (NE, NE)	0.4982 (0.0304, 8.1731) 0.6255	0.6188	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.0976
Yes	37	5 (13.5)	32 (86.5)	24.4 (NE, NE)	13	0	13 (100)	NE (NE, NE)	NE (NE, NE) 0.9967	0.3833	
No	334	15 (4.5)	319 (95.5)	NE (NE, NE)	159	8 (5.0)	151 (95.0)	NE (NE, NE)	0.5513 (0.2285, 1.3301) 0.1851	0.1793	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline CNS metastases											0.1251
Yes	24	4 (16.7)	20 (83.3)	24.4 (NE, NE)	7	0	7 (100)	NE (NE, NE)	NE (NE, NE) 0.9968	0.3712	
No	347	16 (4.6)	331 (95.4)	NE (NE, NE)	165	8 (4.8)	157 (95.2)	NE (NE, NE)	0.5552 (0.2317, 1.3308) 0.1871	0.1815	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.7382
Normal Function	201	11 (5.5)	190 (94.5)	NE (24.4, NE)	80	3 (3.8)	77 (96.3)	NE (NE, NE)	0.8835 (0.2376, 3.2854) 0.8534	0.8533	
Mild Impairment	123	6 (4.9)	117 (95.1)	NE (NE, NE)	65	4 (6.2)	61 (93.8)	NE (NE, NE)	0.3625 (0.0936, 1.4033) 0.1417	0.1263	
Moderate Impairment	41	2 (4.9)	39 (95.1)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	0.9064 (0.0815, 10.0846) 0.9363	0.9363	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.1520
Normal Function	170	9 (5.3)	161 (94.7)	NE (NE, NE)	88	2 (2.3)	86 (97.7)	NE (NE, NE)	1.5444 (0.3306, 7.2140) 0.5805	0.5780	
Mild Impairment	194	10 (5.2)	184 (94.8)	NE (24.4, NE)	82	6 (7.3)	76 (92.7)	NE (NE, NE)	0.3223 (0.1072, 0.9694) 0.0439	0.0348	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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 Run date: 13SEP2022 – 18:59; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_AESEVSOCPT10PAT\_2\_SAS.rtf



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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.2245
Yes	331	18 (5.4)	313 (94.6)	NE (24.4, NE)	146	8 (5.5)	138 (94.5)	NE (NE, NE)	0.6184 (0.2635, 1.4514) 0.2696	0.2658	
No	40	2 (5.0)	38 (95.0)	NE (18.1, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9972	0.6225	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.8583
Positive	329	14 (4.3)	315 (95.7)	NE (24.4, NE)	152	6 (3.9)	146 (96.1)	NE (NE, NE)	0.5501 (0.2031, 1.4895)	0.2332	
Negative	42	6 (14.3)	36 (85.7)	NE (NE, NE)	20	2 (10.0)	18 (90.0)	NE (NE, NE)	1.0393 (0.2066, 5.2270)	0.9659	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
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SOC: Respiratory, thoracic and mediastinal disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) (months) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.7478
Positive	331	15 (4.5)	316 (95.5)	NE (24.4, NE)	155	6 (3.9)	149 (96.1)	NE (NE, NE)	0.6493 (0.2441, 1.7276)	0.3841	
Negative	40	5 (12.5)	35 (87.5)	NE (11.1, NE)	17	2 (11.8)	15 (88.2)	NE (NE, NE)	0.5556 (0.0981, 3.1471)	0.4958	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
HER2 status											0.6609
HER2 IHC 1+	214	3 (1.4)	211 (98.6)	NE (NE, NE)	100	6 (6.0)	94 (94.0)	NE (NE, NE)	0.1377 (0.0325, 0.5829) 0.0071	0.0021	
HER2 IHC 2+/ISH Negative	157	4 (2.5)	153 (97.5)	NE (NE, NE)	72	5 (6.9)	67 (93.1)	NE (NE, NE)	0.2301 (0.0594, 0.8910) 0.0334	0.0214	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of prior lines of chemotherapy in a metastatic setting											0.1303
1	220	3 (1.4)	217 (98.6)	NE (NE, NE)	94	8 (8.5)	86 (91.5)	NE (NE, NE)	0.0947 (0.0239, 0.3751) 0.0008	<0.0001	
>=2	150	4 (2.7)	146 (97.3)	NE (NE, NE)	78	3 (3.8)	75 (96.2)	NE (NE, NE)	0.4381 (0.0927, 2.0712) 0.2977	0.2858	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Prior CDK4/6											0.4145
Yes	233	3 (1.3)	230 (98.7)	NE (NE, NE)	112	7 (6.3)	105 (93.8)	NE (NE, NE)	0.1346 (0.0333, 0.5432) 0.0048	0.0012	
No	98	3 (3.1)	95 (96.9)	NE (NE, NE)	43	3 (7.0)	40 (93.0)	NE (NE, NE)	0.2802 (0.0546, 1.4377) 0.1273	0.1053	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											0.3938
<65	289	7 (2.4)	282 (97.6)	NE (NE, NE)	126	10 (7.9)	116 (92.1)	NE (NE, NE)	0.1647 (0.0594, 0.4565) 0.0005	0.0001	
>=65	82	0	82 (100)	NE (NE, NE)	46	1 (2.2)	45 (97.8)	NE (NE, NE)	0.0000 (0.0000, ) 0.9976	0.1818	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Age											0.9993
<75	357	7 (2.0)	350 (98.0)	NE (NE, NE)	163	11 (6.7)	152 (93.3)	NE (NE, NE)	0.1637 (0.0603, 0.4443) 0.0004	<0.0001	
>=75	14	0	14 (100)	NE (NE, NE)	9	0	9 (100)	NE (NE, NE)	NE (NE, NE) NE		

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Race											0.8757
White	175	4 (2.3)	171 (97.7)	NE (NE, NE)	85	6 (7.1)	79 (92.9)	NE (NE, NE)	0.2225 (0.0609, 0.8127) 0.0230	0.0134	
Non-White	196	3 (1.5)	193 (98.5)	NE (NE, NE)	86	5 (5.8)	81 (94.2)	NE (NE, NE)	0.1241 (0.0270, 0.5711) 0.0074	0.0022	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Region											0.0751
Asia	147	2 (1.4)	145 (98.6)	NE (NE, NE)	63	4 (6.3)	59 (93.7)	NE (NE, NE)	0.0899 (0.0144, 0.5596) 0.0098	0.0023	
North America	58	4 (6.9)	54 (93.1)	NE (NE, NE)	28	1 (3.6)	27 (96.4)	NE (5.8, NE)	0.8237 (0.0858, 7.9060) 0.8665	0.8664	
Europe + Israel	166	1 (0.6)	165 (99.4)	NE (NE, NE)	81	6 (7.4)	75 (92.6)	NE (NE, NE)	0.0756 (0.0091, 0.6283) 0.0168	0.0019	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

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[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
ECOG PS											
0	199	2 (1.0)	197 (99.0)	NE (NE, NE)	95	5 (5.3)	90 (94.7)	NE (NE, NE)	0.1175 (0.0220, 0.6278) 0.0123	0.0031	0.4723
1	172	5 (2.9)	167 (97.1)	NE (NE, NE)	77	6 (7.8)	71 (92.2)	NE (NE, NE)	0.2062 (0.0577, 0.7375) 0.0152	0.0084	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Number of lines of endocrine therapy received in the metastatic setting(1/2)											0.6533
0	60	1 (1.7)	59 (98.3)	NE (NE, NE)	31	4 (12.9)	27 (87.1)	NE (5.3, NE)	0.0478 (0.0043, 0.5353) 0.0136	0.0020	
1	107	2 (1.9)	105 (98.1)	NE (NE, NE)	48	3 (6.3)	45 (93.8)	NE (NE, NE)	0.2231 (0.0365, 1.3625) 0.1042	0.0764	
2	114	3 (2.6)	111 (97.4)	NE (NE, NE)	50	2 (4.0)	48 (96.0)	NE (NE, NE)	0.4746 (0.0760, 2.9640) 0.4252	0.4153	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]
	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Number of lines of endocrine therapy received in the metastatic setting(2/2) >=3	90 (1.1)	89 (98.9)	NE (NE, NE)	43 (4.7)	41 (95.3)	NE (5.8, NE)	0.1396 (0.0118, 1.6506) 0.1182	0.0735	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	p-value [d]
Best Response to last prior cancer systemic therapy											0.0269
PD	173	4 (2.3)	169 (97.7)	NE (NE, NE)	77	5 (6.5)	72 (93.5)	NE (NE, NE)	0.2238 (0.0562, 0.8906)	0.0215	
PR	48	2 (4.2)	46 (95.8)	NE (NE, NE)	21	0	21 (100)	NE (NE, NE)	0.0336 (NE, NE)	0.4997	
SD	82	0	82 (100)	NE (NE, NE)	54	5 (9.3)	49 (90.7)	NE (NE, NE)	0.0000 (0.0000, )	0.0025	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 18:59; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_AEESVSOCPT10PAT\_2\_SAS.rf

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Reported history of CNS metastases											0.3798
Yes	37	2 (5.4)	35 (94.6)	NE (NE, NE)	13	1 (7.7)	12 (92.3)	NE (NE, NE)	0.4792 (0.0404, 5.6843) 0.5599	0.5517	
No	334	5 (1.5)	329 (98.5)	NE (NE, NE)	159	10 (6.3)	149 (93.7)	NE (NE, NE)	0.1410 (0.0462, 0.4298) 0.0006	<0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)			TPC (N=172)			T-DXd vs TPC		Interaction p-value [d]		
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]		Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]
Baseline CNS metastases											
Yes	24	2 (8.3)	22 (91.7)	NE (11.6, NE)	7	0	7 (100)	NE (NE, NE)	0.9975	0.5045	0.0492
No	347	5 (1.4)	342 (98.6)	NE (NE, NE)	165	11 (6.7)	154 (93.3)	NE (NE, NE)	0.1284 (0.0428, 0.3849)	0.0002	<0.0001

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Renal function at baseline											0.4705
Normal Function	201	6 (3.0)	195 (97.0)	NE (NE, NE)	80	9 (11.3)	71 (88.8)	NE (NE, NE)	0.1125 (0.0359, 0.3525) 0.0002	<0.0001	
Mild Impairment	123	0	123 (100)	NE (NE, NE)	65	1 (1.5)	64 (98.5)	NE (NE, NE)	0.0000 (0.0000, ) 0.9977	0.1590	
Moderate Impairment	41	1 (2.4)	40 (97.6)	NE (NE, NE)	23	1 (4.3)	22 (95.7)	NE (NE, NE)	0.5360 (0.0335, 8.5760) 0.6594	0.6542	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hepatic function at baseline											0.7584
Normal Function	170	4 (2.4)	166 (97.6)	NE (NE, NE)	88	6 (6.8)	82 (93.2)	NE (NE, NE)	0.2388 (0.0649, 0.8784) 0.0312	0.0203	
Mild Impairment	194	3 (1.5)	191 (98.5)	NE (NE, NE)	82	5 (6.1)	77 (93.9)	NE (NE, NE)	0.1237 (0.0274, 0.5589) 0.0066	0.0017	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Baseline visceral disease											0.1372
Yes	331	6 (1.8)	325 (98.2)	NE (NE, NE)	146	11 (7.5)	135 (92.5)	NE (NE, NE)	0.1523 (0.0543, 0.4271) 0.0003	<0.0001	
No	40	1 (2.5)	39 (97.5)	NE (NE, NE)	26	0	26 (100)	NE (NE, NE)	NE (NE, NE) 0.9984	0.7963	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

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SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (IXRS)											0.2606
Positive	329	5 (1.5)	324 (98.5)	NE (NE, NE)	152	10 (6.6)	142 (93.4)	NE (NE, NE)	0.1371 (0.0451, 0.4166) 0.0005	<0.0001	
Negative	42	2 (4.8)	40 (95.2)	NE (NE, NE)	20	1 (5.0)	19 (95.0)	NE (NE, NE)	0.4939 (0.0309, 7.8964) 0.6179	0.6106	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable

[a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.

[c] Two-sided p-value from unstratified log-rank test.

[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 18:59; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_AESEVSOCPT10PAT\_2\_SAS.rtf

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DE.T.4.12.2 - Severe Treatment-emergent adverse events (NCI CTCAE grade >=3) by system organ class (SOC) and preferred term (PT) observed for >= 10 patients in at least one arm and >= 1% of the patients in at least one arm - Time-to-event analysis - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

SOC: Nervous system disorders; PT: Any PT

Subgroup	T-DXd (N=371)				TPC (N=172)				T-DXd vs TPC		Interaction p-value [d]
	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Nsub	No. of subjects with events (%)	No. of subjects censored (%)	Median (95% CI) [a]	Hazard Ratio (95% CI) p-value [b]	Unstratified log-rank p-value [c]	
Hormon receptor status (derived)											0.7885
Positive	331	6 (1.8)	325 (98.2)	NE (NE, NE)	155	10 (6.5)	145 (93.5)	NE (NE, NE)	0.1742 (0.0610, 0.4972)	0.0003	
Negative	40	1 (2.5)	39 (97.5)	NE (NE, NE)	17	1 (5.9)	16 (94.1)	NE (NE, NE)	0.0000 (0.0000, ) 0.9978	0.1299	

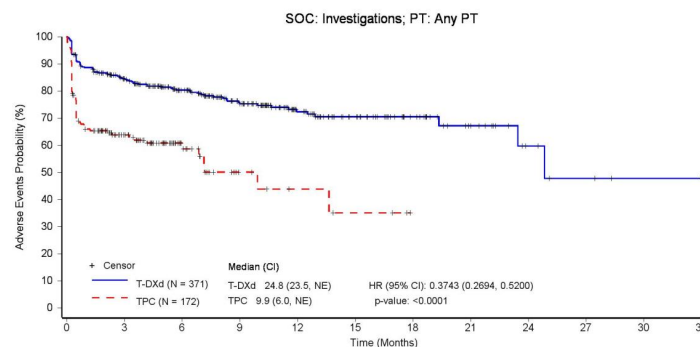
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; %: proportion of number of subjects in subgroup category; CI: confidence interval; NE: not estimable  
 [a] Median time to first event is from Kaplan-Meier estimate. Confidence Interval for median was computed using the Brookmeyer-Crowley method.  
 [b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the Wald test. p-value: two-sided p-value based on the Wald test.  
 [c] Two-sided p-value from unstratified log-rank test.  
 [d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the Wald test.

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 18:59; Program name: T4\_AESOCPT10PAT\_2\_SAS.sas; Output name: T4\_AESEVSOCPT10PAT\_2\_SAS.rtf

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DE.F.4.12.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	275	203	145	85	55	31	15	6	3	1	0
TPC (N = 172)	172	70	28	9	5	3	0	0	0	0	0	0

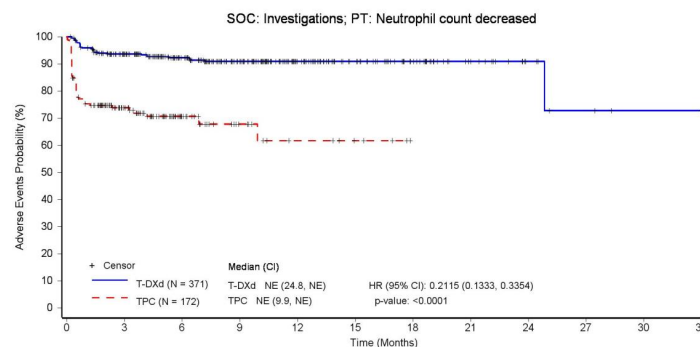
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:02; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESEVSOCPT10PAT\_3\_SAS.rtf

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DE.F.4.12.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	295	222	162	99	65	39	17	7	3	1	0
TPC (N = 172)	172	78	31	14	7	4	0	0	0	0	0	0

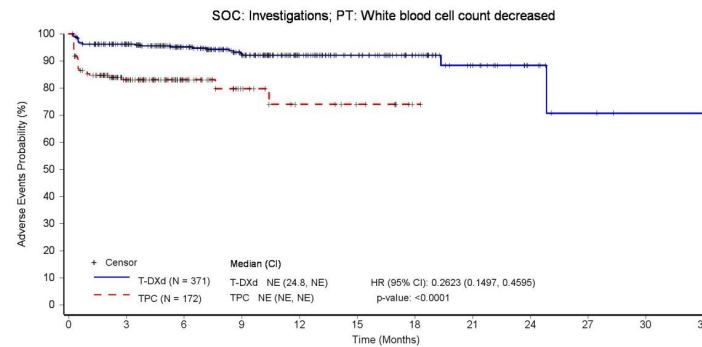
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:02; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESEVSOCPT10PAT\_3\_SAS.rtf

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DE.F.4.12.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	303	227	165	102	69	41	19	8	3	1	0
TPC (N = 172)	172	89	40	18	10	7	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

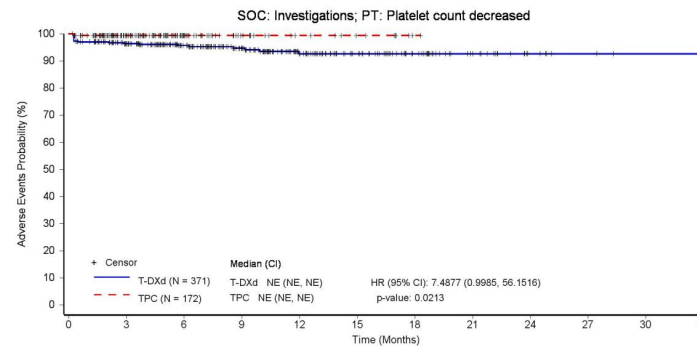
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 Run date: 21OCT2022 – 18:02; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESEVSOCPT10PAT\_3\_SAS.rtf



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DE.F.4.12.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	T-DXd (N = 371)	TPC (N = 172)
0	371	172
3	303	106
6	229	44
9	169	20
12	106	11
15	70	7
18	41	1
21	19	0
24	7	0
27	3	0
30	1	0
33	0	0

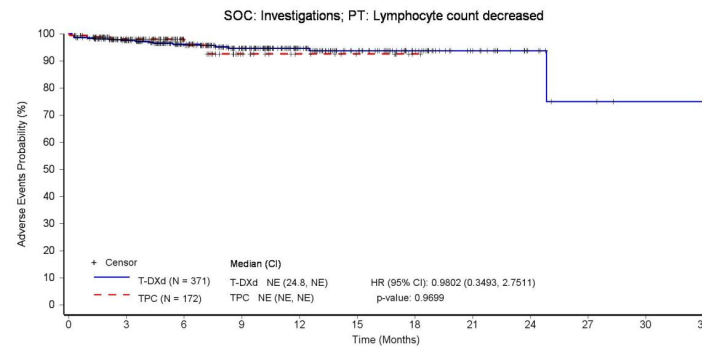
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:02; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESEVSOCPT10PAT\_3\_SAS.rtf

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DE.F.4.12.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	T-DXd (N = 371)	TPC (N = 172)
0	371	172
3	308	105
6	231	43
9	169	18
12	108	10
15	70	6
18	41	1
21	20	0
24	8	0
27	3	0
30	1	0
33	0	0

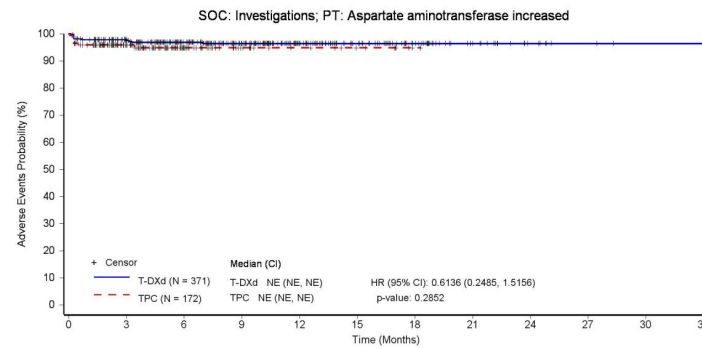
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.12.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	T-DXd (N = 371)	TPC (N = 172)
0	371	172
3	309	103
6	233	42
9	171	18
12	109	11
15	71	7
18	42	1
21	19	0
24	8	0
27	3	0
30	1	0
33	0	0

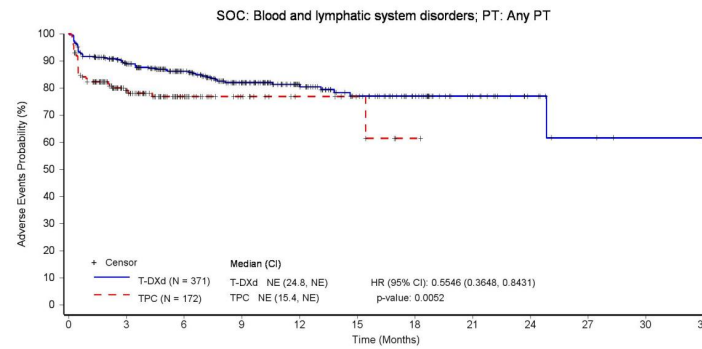
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:02; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESEVSOCPT10PAT\_3\_SAS.rtf

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DE.F.4.12.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	282	207	145	91	59	38	18	8	3	1	0
TPC (N = 172)	172	83	34	16	8	5	1	0	0	0	0	0

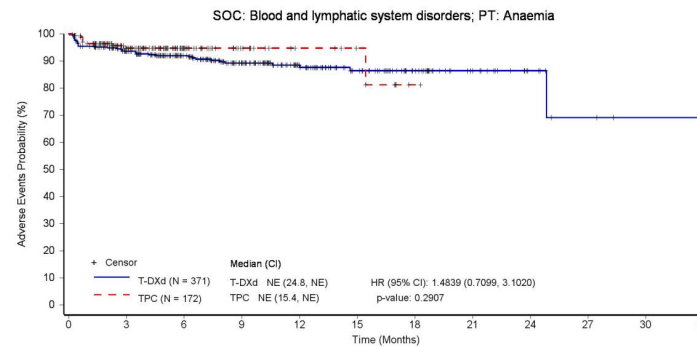
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:02; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESEVSOCPT10PAT\_3\_SAS.rtf

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DE.F.4.12.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	296	222	159	102	68	41	19	8	3	1	0
TPC (N = 172)	172	102	42	19	10	7	1	0	0	0	0	0

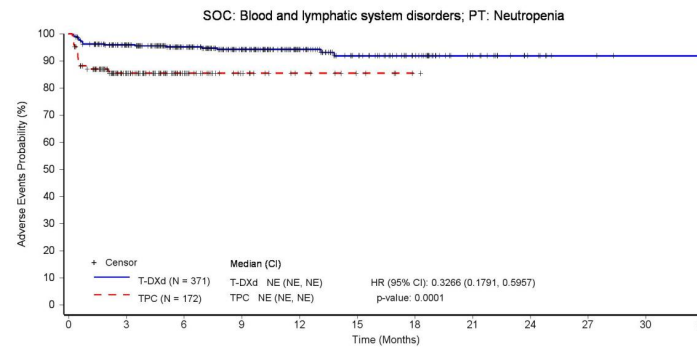
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:02; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESEVSOCPT10PAT\_3\_SAS.rtf

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DE.F.4.12.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	300	223	160	99	63	41	19	8	3	1	0
TPC (N = 172)	172	89	38	17	9	5	1	0	0	0	0	0

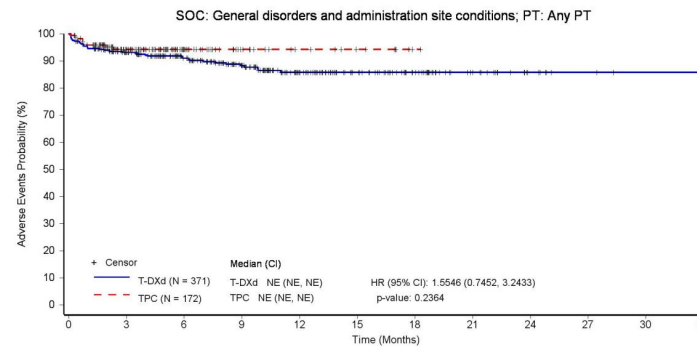
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:02; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESEVSOCPT10PAT\_3\_SAS.rtf

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DE.F.4.12.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	295	224	166	106	70	43	20	8	3	1	0
TPC (N = 172)	172	100	42	19	11	7	1	0	0	0	0	0

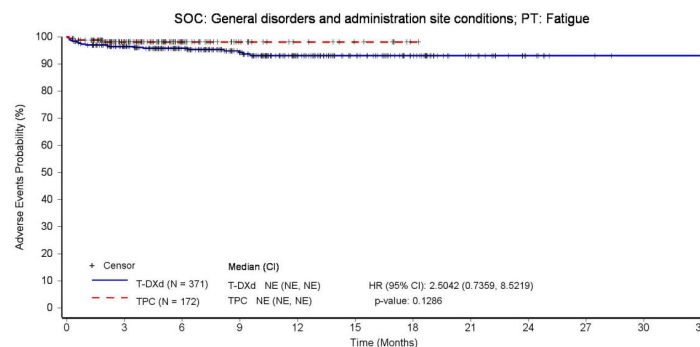
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.12.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	303	232	169	108	71	43	20	8	3	1	0
TPC (N = 172)	172	104	44	20	11	7	1	0	0	0	0	0

Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

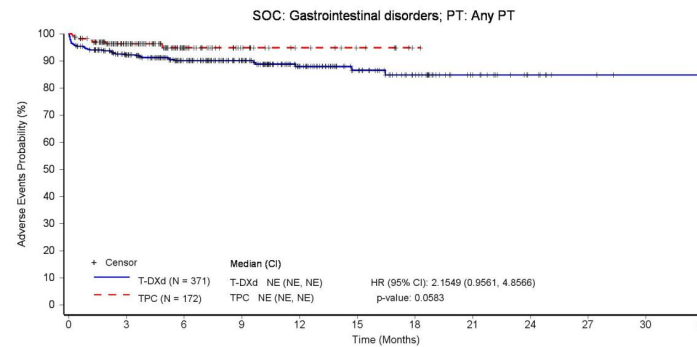
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DE.F.4.12.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	289	217	158	96	61	39	18	8	3	1	0
TPC (N = 172)	172	105	42	20	11	7	1	0	0	0	0	0

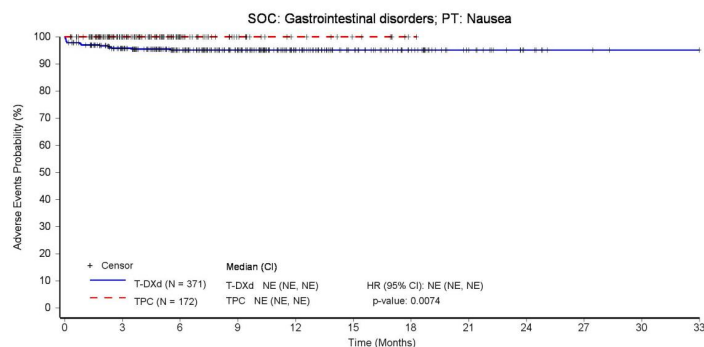
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.12.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	299	226	166	104	67	41	19	8	3	1	0
TPC (N = 172)	172	107	44	20	11	7	1	0	0	0	0	0

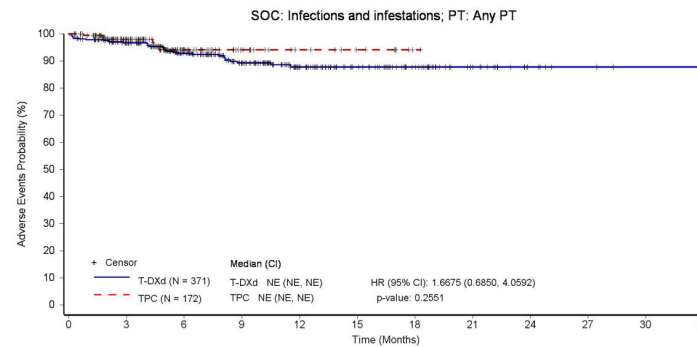
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.12.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	310	229	162	99	66	41	19	7	3	1	0
TPC (N = 172)	172	105	42	20	11	7	1	0	0	0	0	0

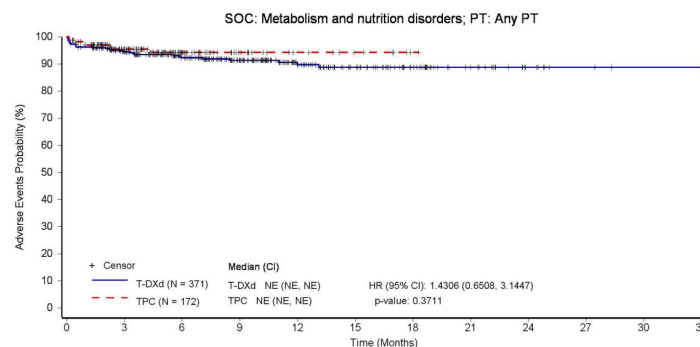
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.12.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	301	225	166	102	68	40	20	8	3	1	0
TPC (N = 172)	172	104	42	19	10	6	1	0	0	0	0	0

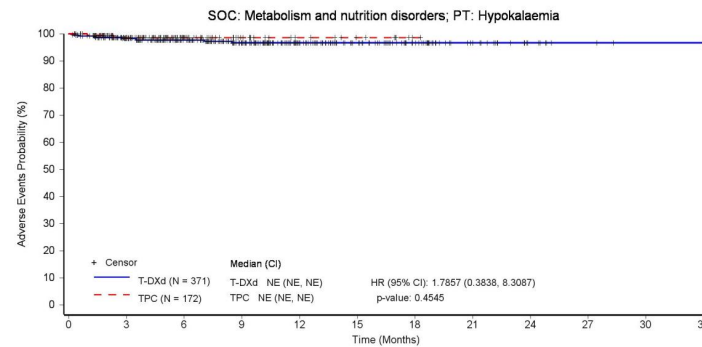
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:02; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESEVSOCPT10PAT\_3\_SAS.rtf

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DE.F.4.12.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	309	234	171	108	72	43	20	8	3	1	0
TPC (N = 172)	172	106	43	20	11	7	1	0	0	0	0	0

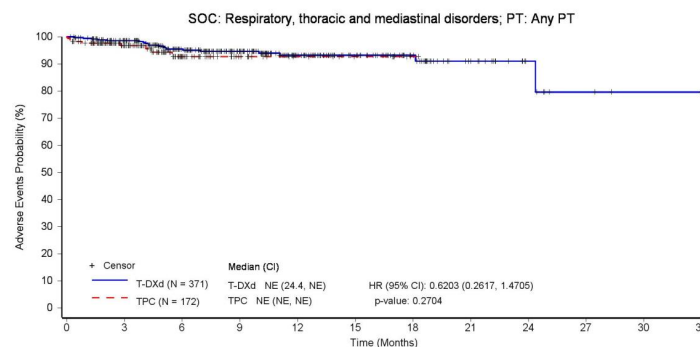
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

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DE.F.4.12.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	312	235	171	107	71	43	20	8	3	1	0
TPC (N = 172)	172	104	43	19	10	6	1	0	0	0	0	0

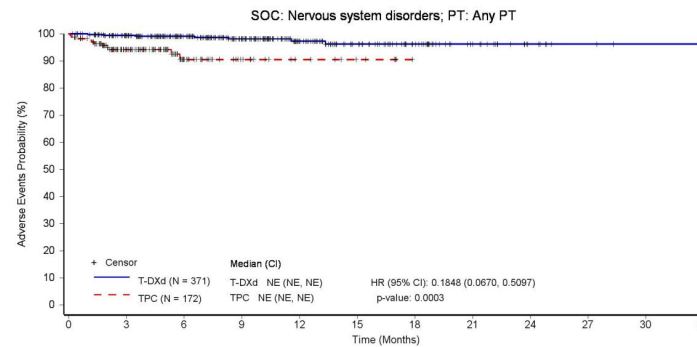
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:02; Program name: F4\_AESOCPT10PER\_3\_SAS.sas; Output name: F4\_AESEVSOCPT10PAT\_3\_SAS.rtf

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DE.F.4.12.3 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 371)	371	313	236	171	107	71	43	20	8	3	1	0
TPC (N = 172)	172	101	38	17	9	5	0	0	0	0	0	0

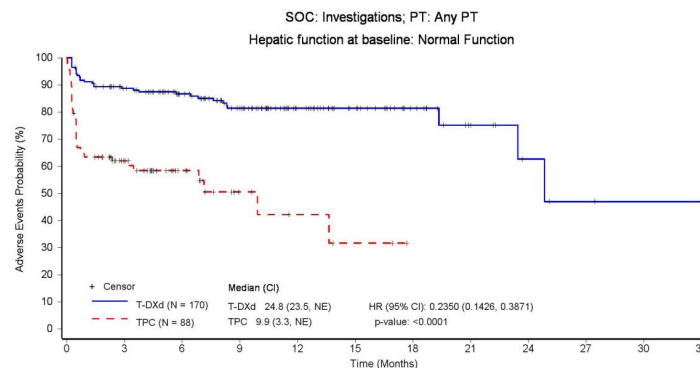
Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 170)	170	139	111	85	51	34	18	8	4	2	1	0
TPC (N = 88)	88	37	18	7	4	2	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

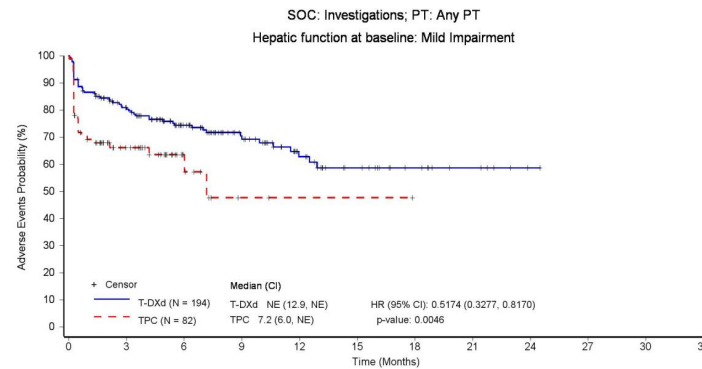
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 Run date: 21OCT2022 – 18:03; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESEVSOCPT10PAT\_4\_SAS.rtf



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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 194)	194	133	90	58	33	20	12	6	1	0	0	0
TPC (N = 82)	82	33	10	2	1	1	0	0	0	0	0	0

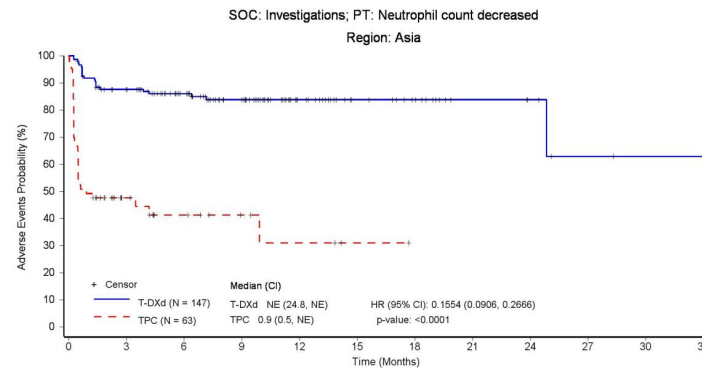
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 147)	147	115	86	65	33	20	15	7	5	2	1	0
TPC (N = 63)	63	16	9	5	3	1	0	0	0	0	0	0

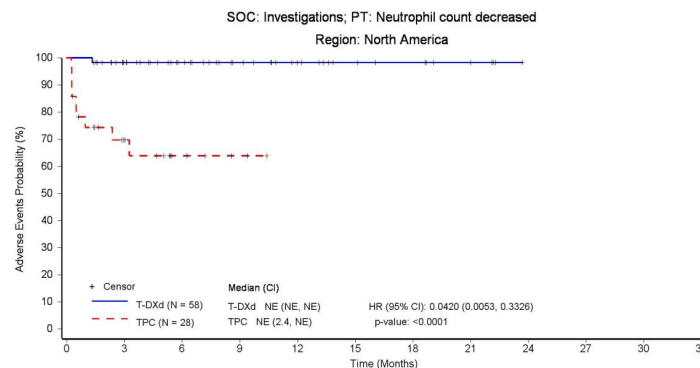
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 58)	58	45	34	25	17	11	8	4	0	0	0	0
TPC (N = 28)	28	13	5	2	0	0	0	0	0	0	0	0

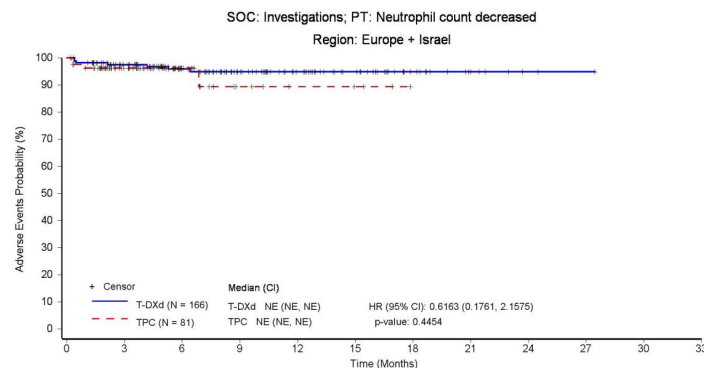
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:03; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESEVSOCPT10PAT\_4\_SAS.rtf

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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 166)	166	135	102	72	49	34	16	6	2	1	0	0
TPC (N = 81)	81	49	17	7	4	3	0	0	0	0	0	0

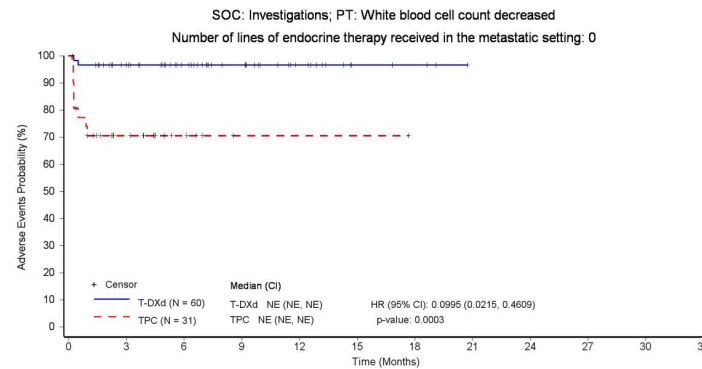
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 60)	60	47	32	22	12	4	3	0	0	0	0	0
TPC (N = 31)	31	13	5	1	1	1	0	0	0	0	0	0

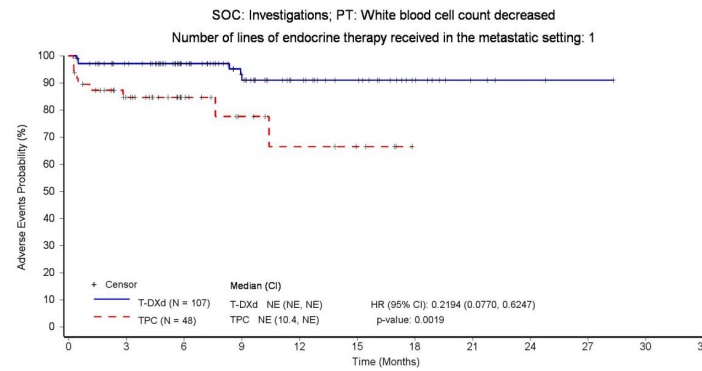
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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 Run date: 21OCT2022 – 18:03; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESEVSOCPT10PAT\_4\_SAS.rtf

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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 107)	107	89	65	44	28	20	10	4	2	1	0	0
TPC (N = 48)	48	30	16	9	6	4	0	0	0	0	0	0

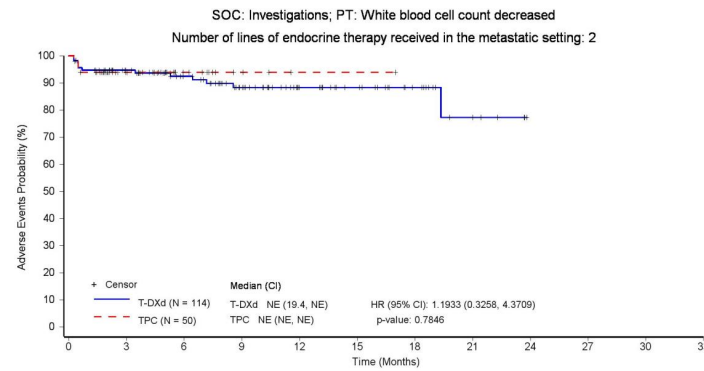
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 114)	114	89	73	55	35	25	14	5	0	0	0	0
TPC (N = 50)	50	27	11	4	1	1	0	0	0	0	0	0

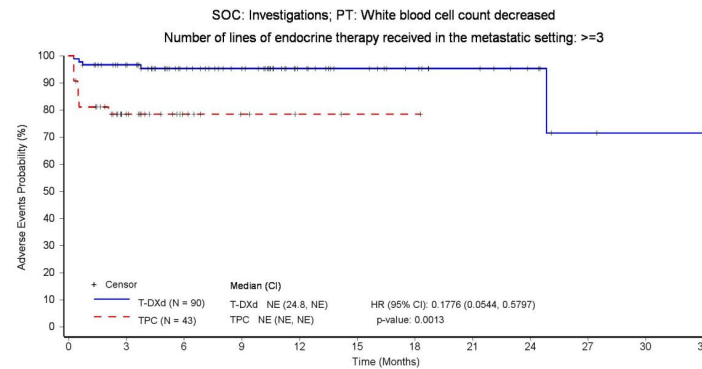
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 90)	90	78	57	44	27	20	14	10	6	2	1	0
TPC (N = 43)	43	19	8	4	2	1	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

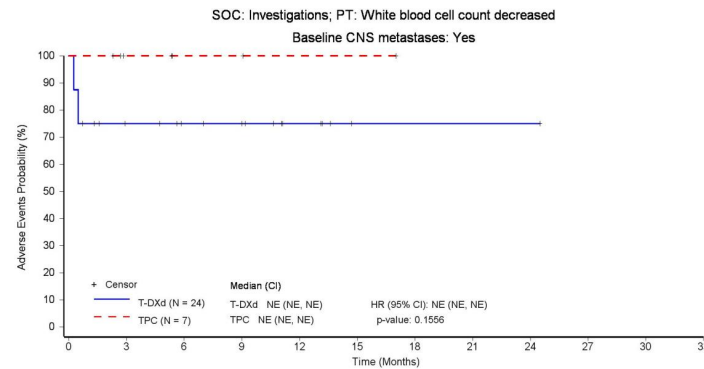
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 Run date: 21OCT2022 – 18:03; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESEVSOCPT10PAT\_4\_SAS.rtf



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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 24)	24	14	11	10	5	1	1	1	1	0	0	0
TPC (N = 7)	7	4	2	2	1	1	0	0	0	0	0	0

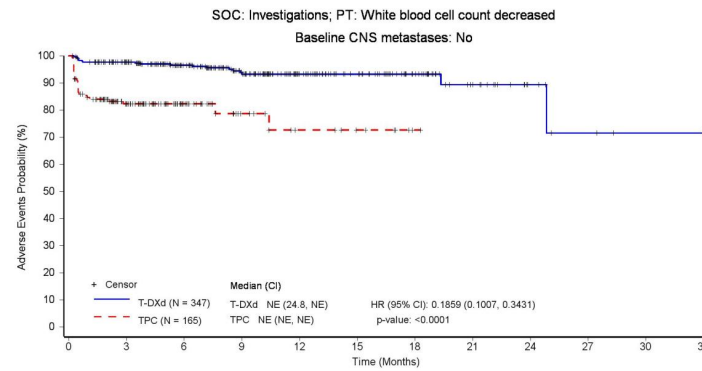
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 347)	347	289	216	155	97	68	40	18	7	3	1	0
TPC (N = 165)	165	85	38	16	9	6	1	0	0	0	0	0

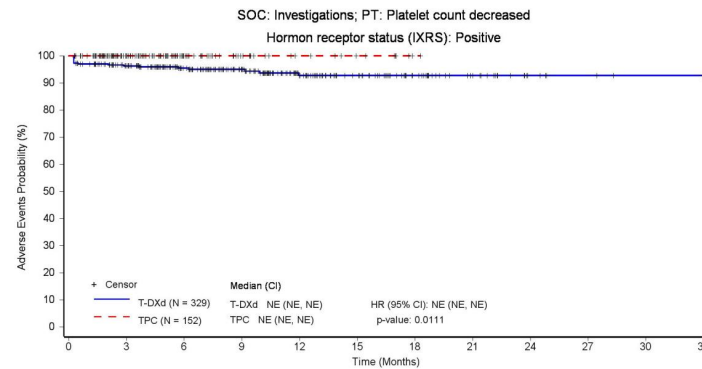
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Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 329)	329	273	209	156	98	65	37	18	6	3	1	0
TPC (N = 152)	152	96	41	20	11	7	1	0	0	0	0	0

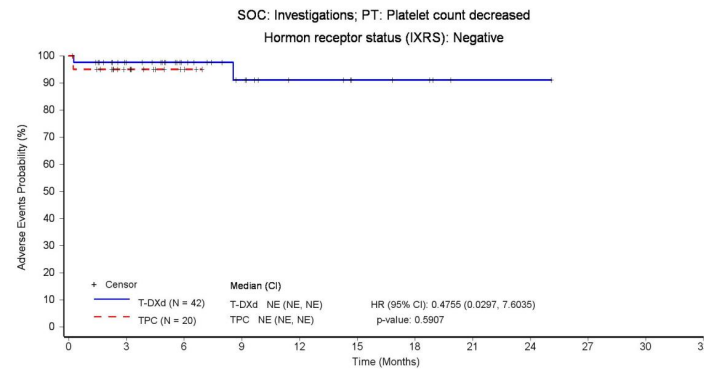
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 42)	42	30	20	13	8	5	4	1	1	0	0	0
TPC (N = 20)	20	11	3	0	0	0	0	0	0	0	0	0

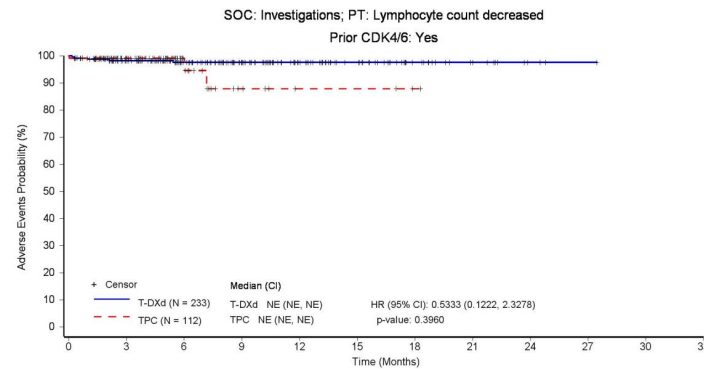
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 21OCT2022 – 18:03; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESEVSOCPT10PAT\_4\_SAS.rtf

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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 233)	233	189	137	96	63	43	21	9	3	1	0	0
TPC (N = 112)	112	66	22	7	3	3	1	0	0	0	0	0

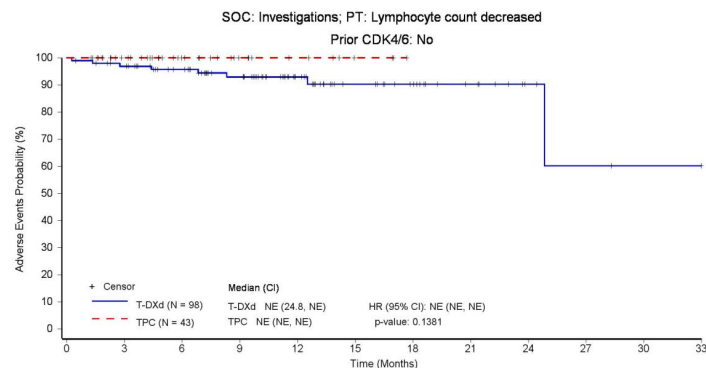
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 98)	98	91	77	63	38	23	17	10	4	2	1	0
TPC (N = 43)	43	32	19	11	7	3	0	0	0	0	0	0

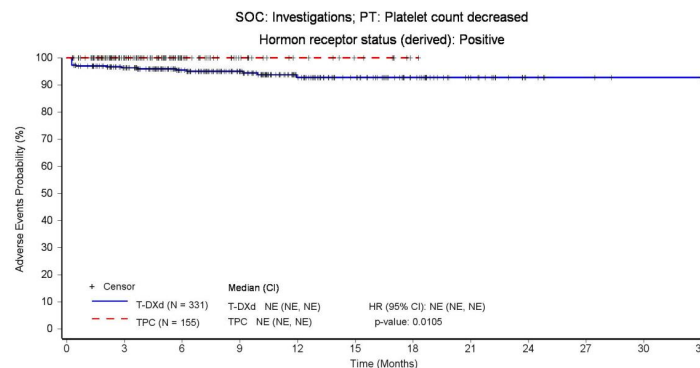
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 331)	331	274	209	157	99	66	38	18	6	3	1	0
TPC (N = 155)	155	98	41	20	11	7	1	0	0	0	0	0

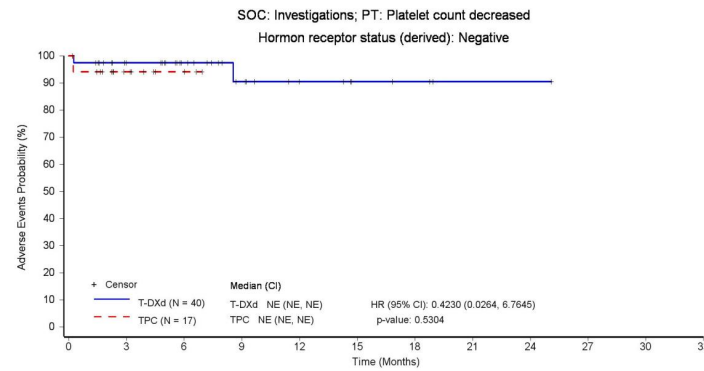
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 40)	40	29	20	12	7	4	3	1	1	0	0	0
TPC (N = 17)	17	8	3	0	0	0	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

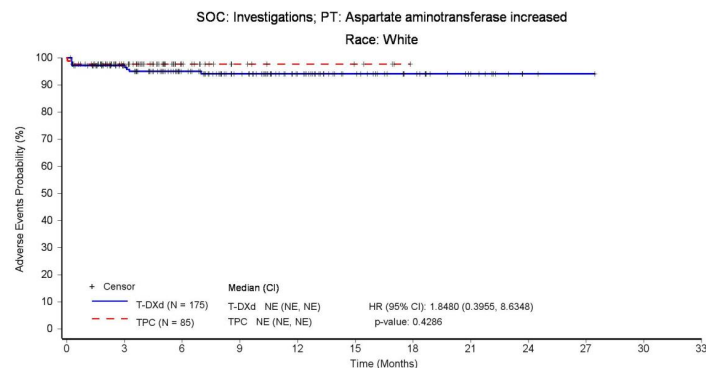
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 175)	175	140	106	79	53	34	20	10	2	1	0	0
TPC (N = 85)	85	49	18	8	5	4	0	0	0	0	0	0

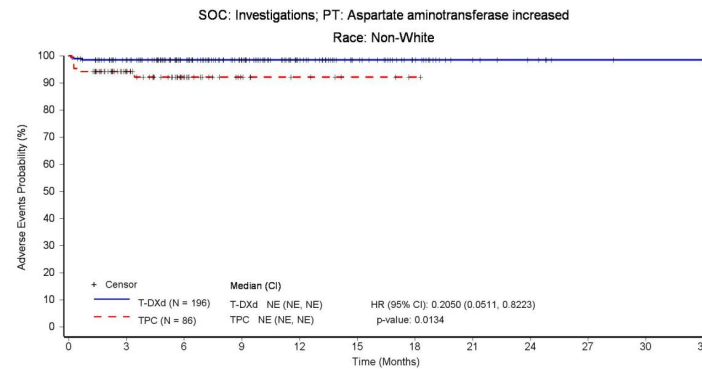
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

Time (Months)	T-DXd (N = 196)	TPC (N = 86)
0	196	86
3	169	53
6	127	24
9	92	10
12	56	6
15	37	3
18	22	1
21	9	0
24	6	0
27	2	0
30	1	0
33	0	0

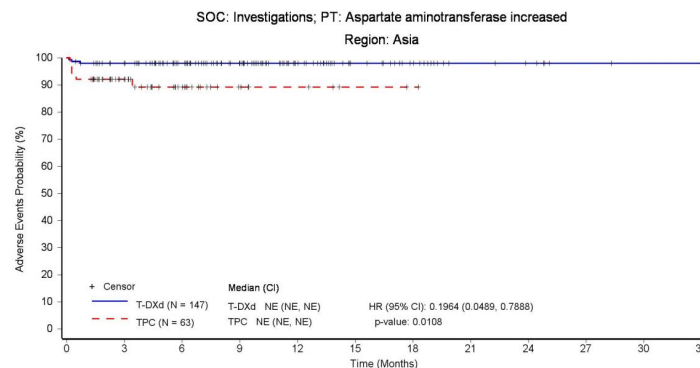
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 147)	147	129	98	74	42	25	17	8	6	2	1	0
TPC (N = 63)	63	37	19	8	5	2	1	0	0	0	0	0

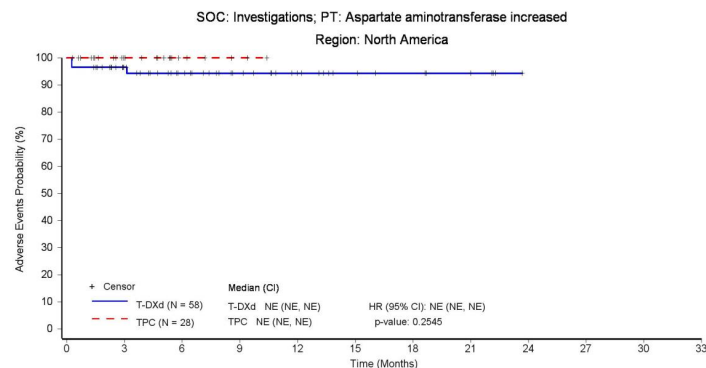
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 58)	58	44	33	24	16	10	7	4	0	0	0	0
TPC (N = 28)	28	15	5	2	0	0	0	0	0	0	0	0

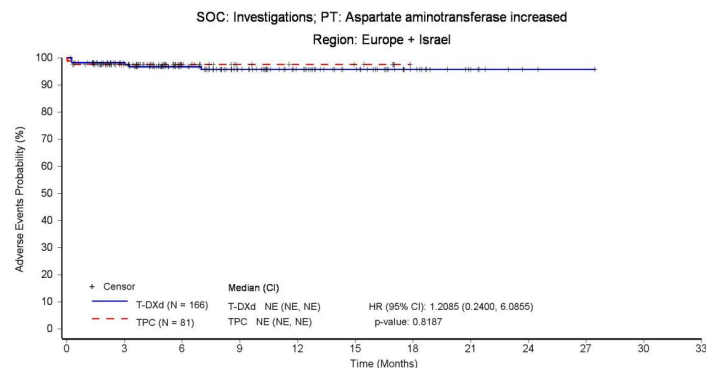
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 166)	166	136	102	73	51	36	18	7	2	1	0	0
TPC (N = 81)	81	51	18	8	6	5	0	0	0	0	0	0

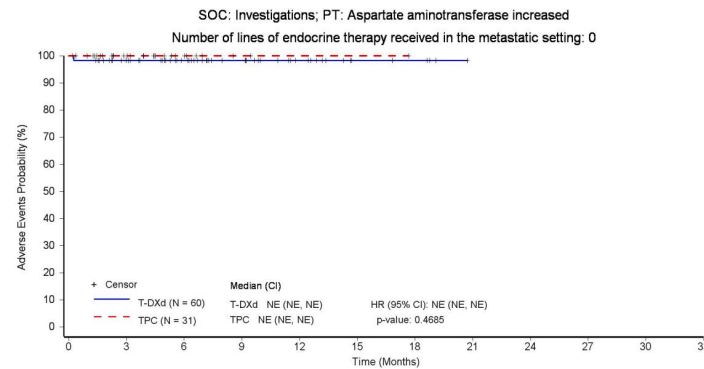
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 60)	60	48	34	23	13	5	4	0	0	0	0	0
TPC (N = 31)	31	18	7	2	1	1	0	0	0	0	0	0

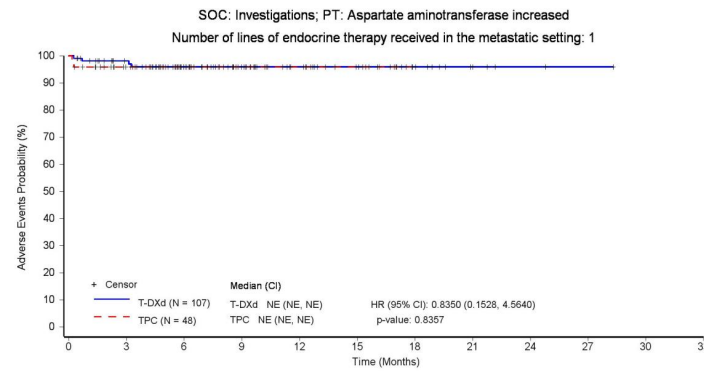
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 107)	107	90	65	46	31	22	11	4	2	1	0	0
TPC (N = 48)	48	34	17	9	7	4	0	0	0	0	0	0

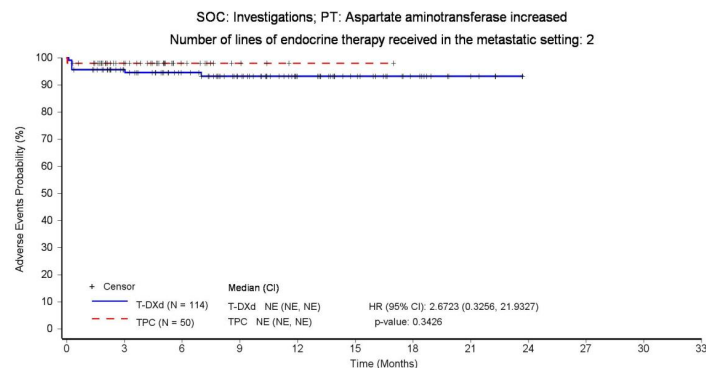
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 114)	114	90	74	57	37	24	13	5	0	0	0	0
TPC (N = 50)	50	30	11	4	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

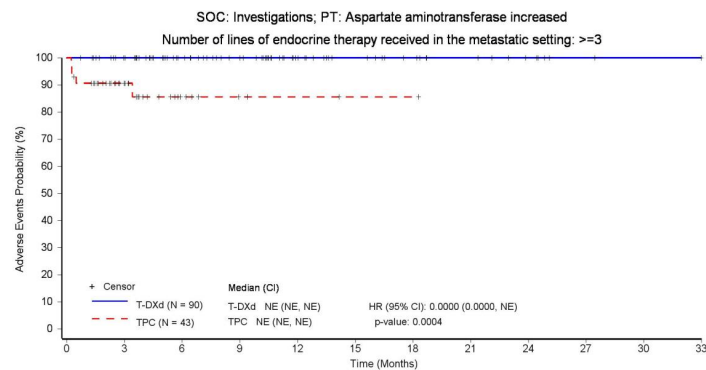
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 90)	90	81	60	45	28	20	14	10	6	2	1	0
TPC (N = 43)	43	21	7	3	2	1	1	0	0	0	0	0

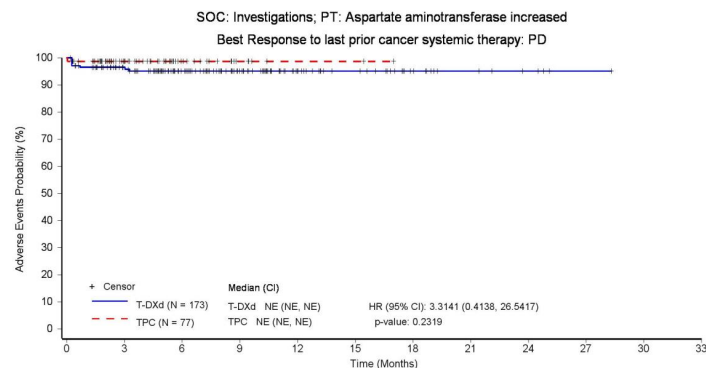
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 173)	173	140	99	69	39	27	14	7	4	1	0	0
TPC (N = 77)	77	45	18	6	2	2	0	0	0	0	0	0

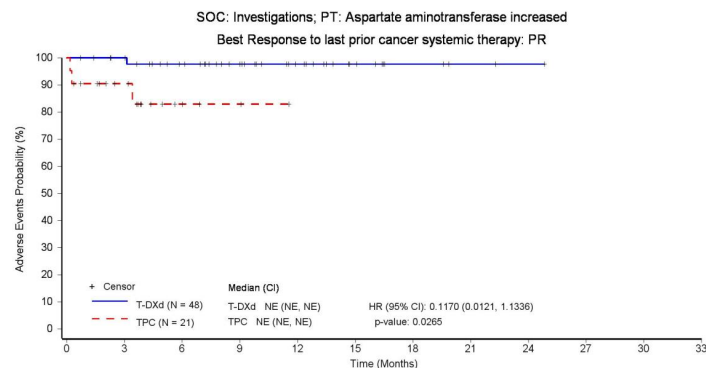
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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 48)	48	44	36	27	17	9	4	2	1	0	0	0
TPC (N = 21)	21	13	4	2	0	0	0	0	0	0	0	0

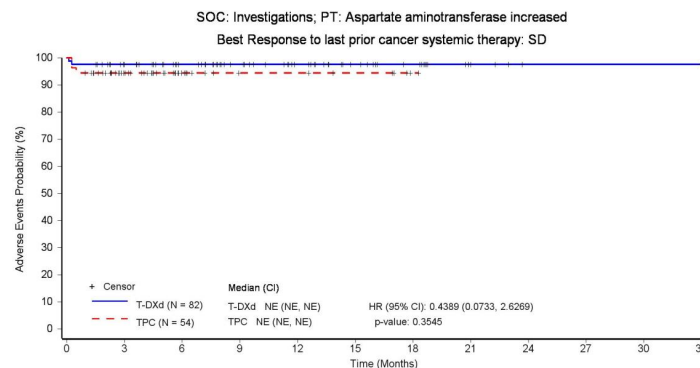
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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 82)	82	66	52	40	30	20	14	4	1	1	1	0
TPC (N = 54)	54	33	15	7	7	5	1	0	0	0	0	0

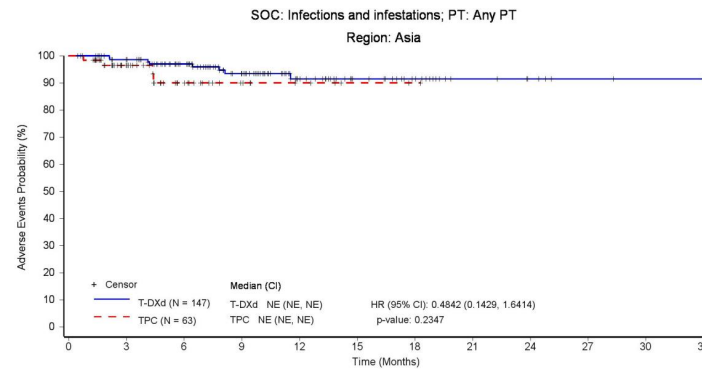
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	T-DXd (N = 147)	TPC (N = 63)
0	147	63
3	131	39
6	99	19
9	71	9
12	39	5
15	25	2
18	17	1
21	8	0
24	5	0
27	2	0
30	1	0
33	0	0

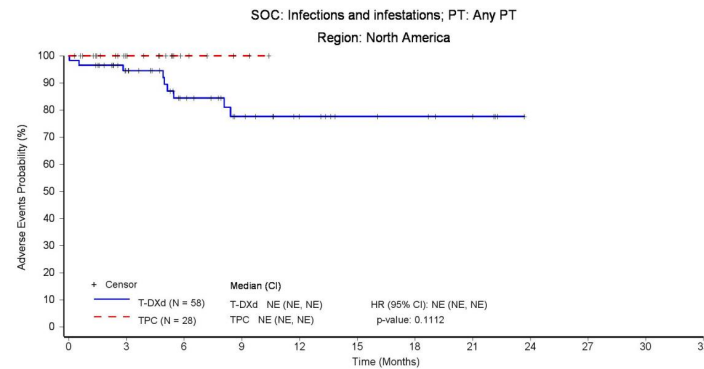
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 58)	58	44	30	21	14	9	7	4	0	0	0	0
TPC (N = 28)	28	15	5	2	0	0	0	0	0	0	0	0

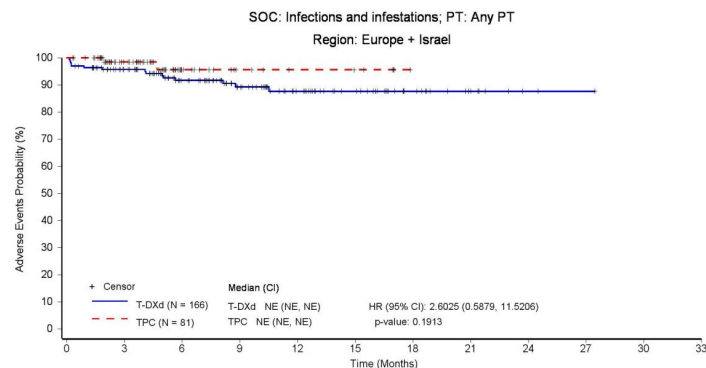
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	T-DXd (N = 166)	TPC (N = 81)
0	166	81
3	135	51
6	100	18
9	70	9
12	46	6
15	32	5
18	17	0
21	7	0
24	2	0
27	1	0
30	0	0
33	0	0

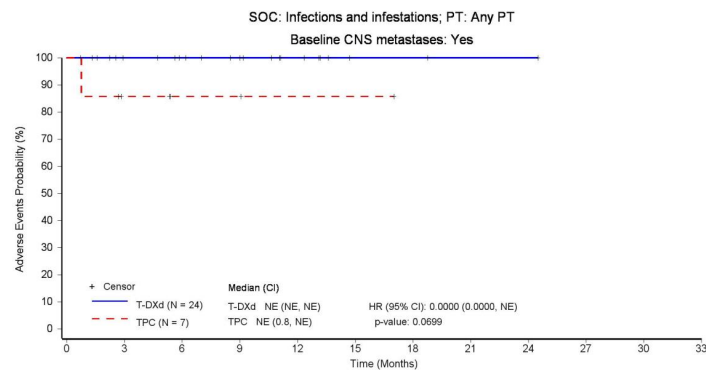
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 24)	24	18	15	12	7	2	2	1	1	0	0	0
TPC (N = 7)	7	4	2	2	1	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

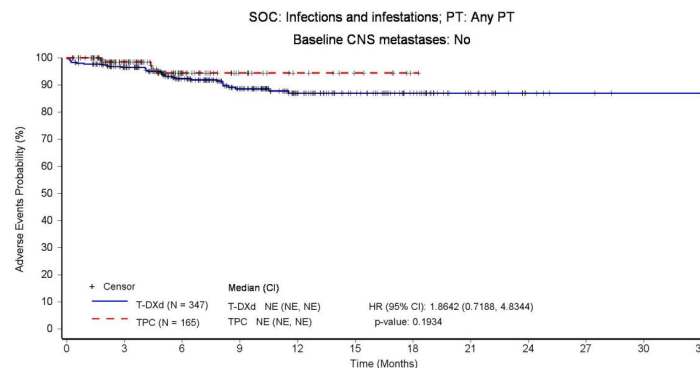
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 347)	347	292	214	150	92	64	39	18	6	3	1	0
TPC (N = 165)	165	101	40	18	10	6	1	0	0	0	0	0

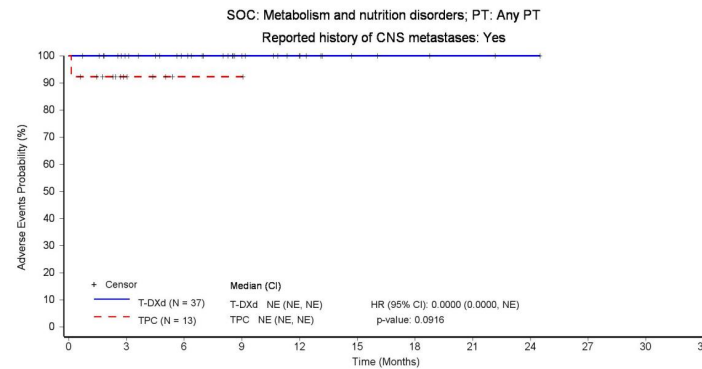
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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 37)	37	30	24	15	9	4	3	2	1	0	0	0
TPC (N = 13)	13	5	1	1	0	0	0	0	0	0	0	0

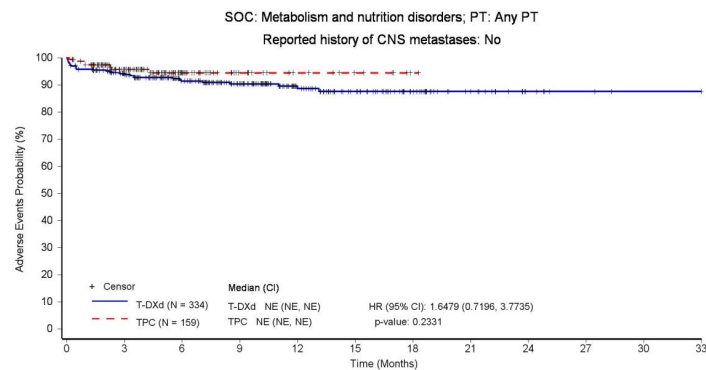
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 334)	334	271	201	151	93	64	37	18	7	3	1	0
TPC (N = 159)	159	99	41	18	10	6	1	0	0	0	0	0

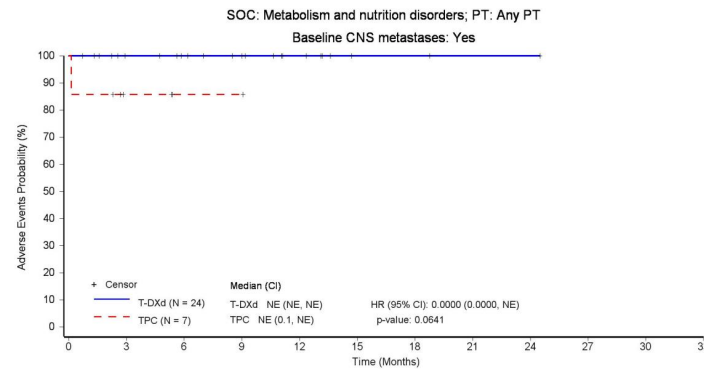
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 24)	24	18	15	12	7	2	2	1	1	0	0	0
TPC (N = 7)	7	3	1	1	0	0	0	0	0	0	0	0

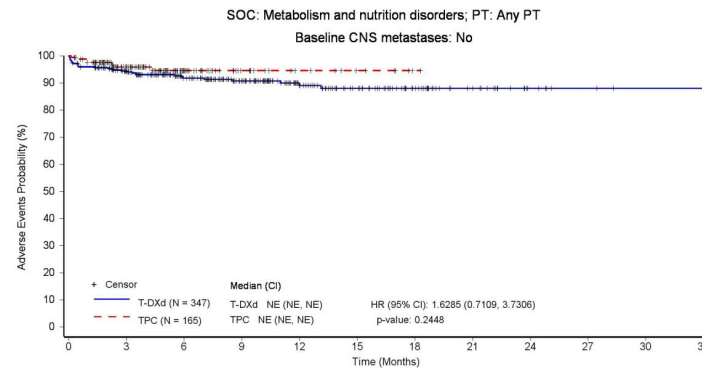
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 347)	347	283	210	154	95	66	38	19	7	3	1	0
TPC (N = 165)	165	101	41	18	10	6	1	0	0	0	0	0

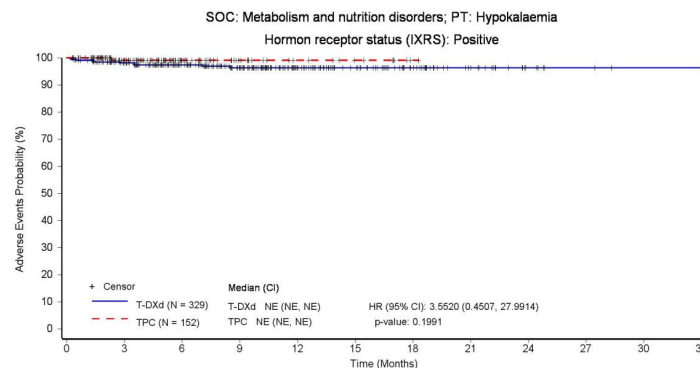
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 329)	329	278	214	158	100	67	39	19	7	3	1	0
TPC (N = 152)	152	94	40	20	11	7	1	0	0	0	0	0

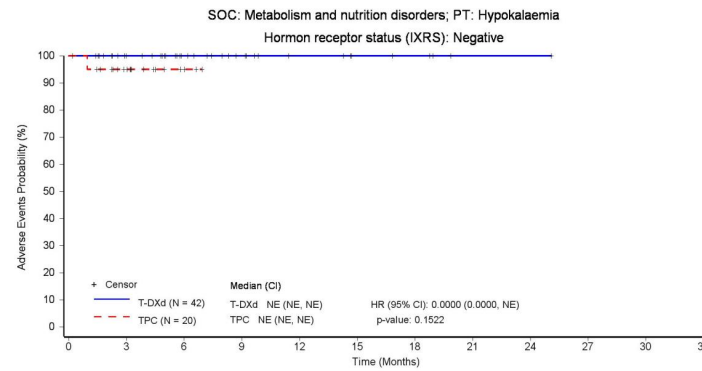
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 42)	42	31	20	13	8	5	4	1	1	0	0	0
TPC (N = 20)	20	12	3	0	0	0	0	0	0	0	0	0

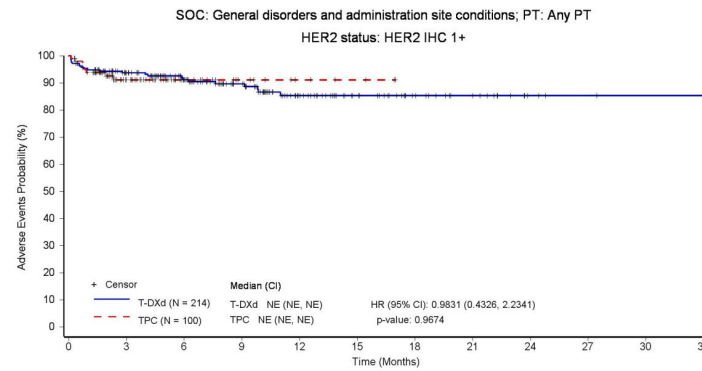
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 214)	214	167	128	97	59	38	23	13	4	2	1	0
TPC (N = 100)	100	54	25	10	5	3	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

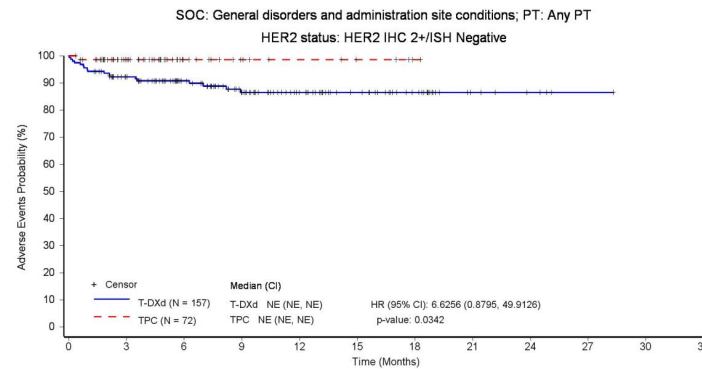
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 157)	157	128	96	69	47	32	20	7	4	1	0	0
TPC (N = 72)	72	46	17	9	6	4	1	0	0	0	0	0

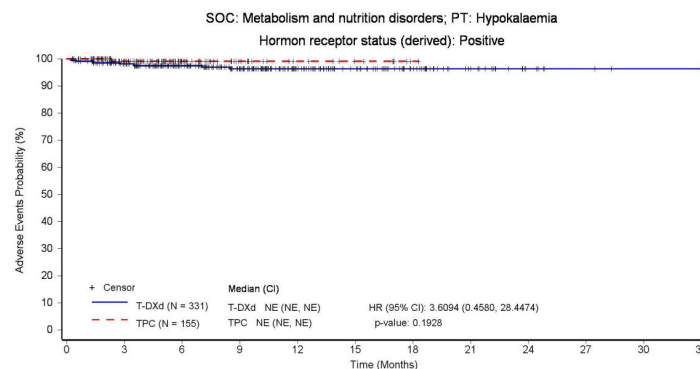
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 331)	331	279	214	159	101	68	40	19	7	3	1	0
TPC (N = 155)	155	97	40	20	11	7	1	0	0	0	0	0

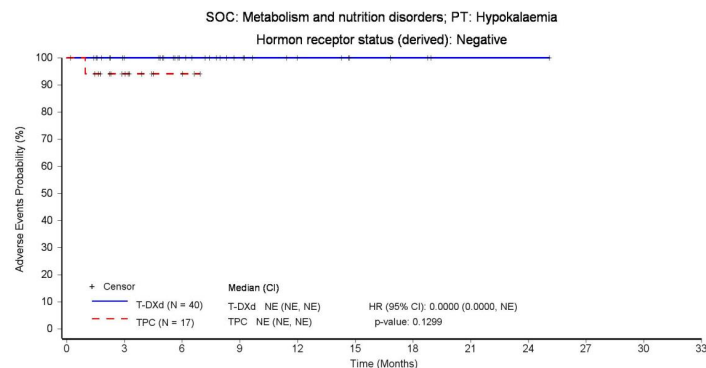
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Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 40)	40	30	20	12	7	4	3	1	1	0	0	0
TPC (N = 17)	17	9	3	0	0	0	0	0	0	0	0	0

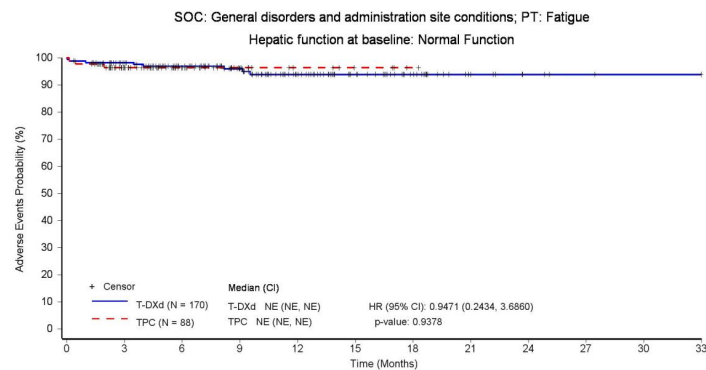
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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 170)	170	152	124	96	61	39	22	8	4	2	1	0
TPC (N = 88)	88	58	28	13	7	4	1	0	0	0	0	0

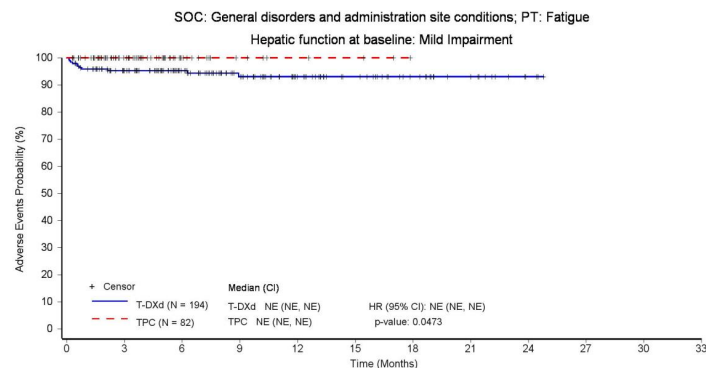
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 194)	194	149	106	71	46	31	20	11	3	0	0	0
TPC (N = 82)	82	46	16	7	4	3	0	0	0	0	0	0

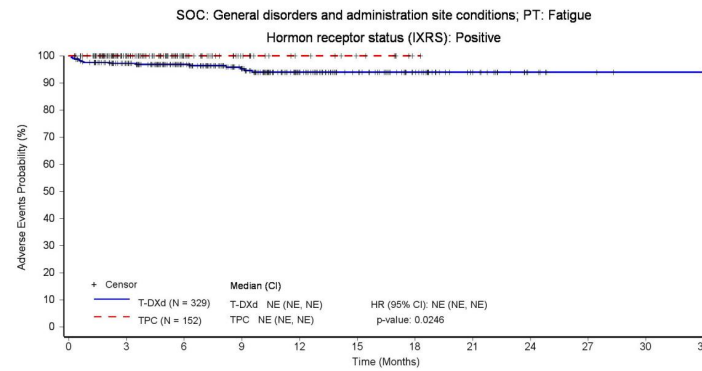
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	T-DXd (N = 329)	TPC (N = 152)
0	329	152
3	275	96
6	213	41
9	157	20
12	100	11
15	66	7
18	39	1
21	19	0
24	7	0
27	3	0
30	1	0
33	0	0

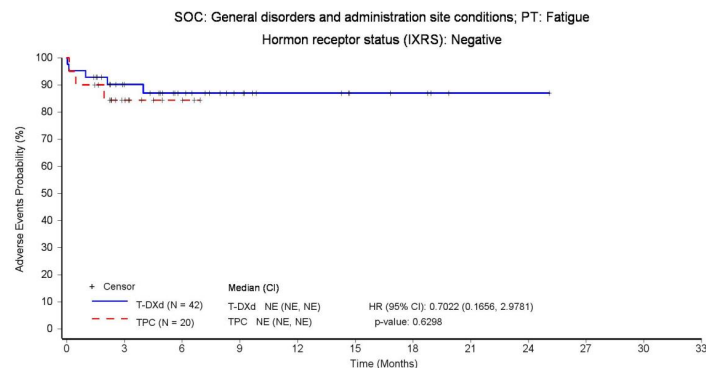
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 42)	42	28	19	12	8	5	4	1	1	0	0	0
TPC (N = 20)	20	9	3	0	0	0	0	0	0	0	0	0

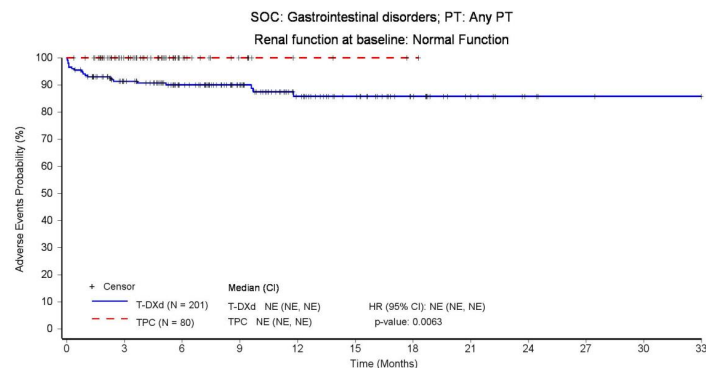
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 201)	201	156	114	83	49	34	20	9	4	2	1	0
TPC (N = 80)	80	49	18	8	3	2	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

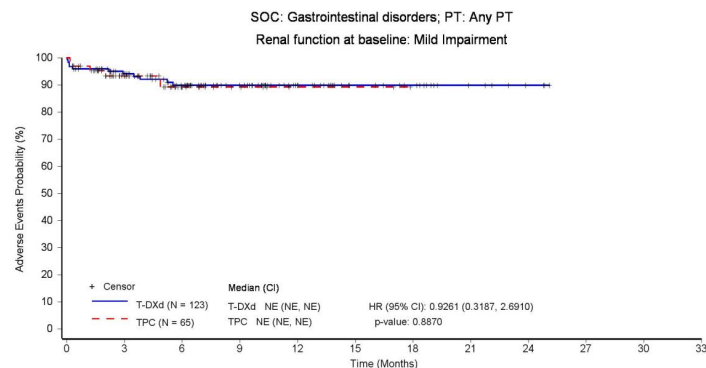
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 Run date: 21OCT2022 – 18:03; Program name: F4\_AESOCPT10PER\_4\_SAS.sas; Output name: F4\_AESEVSOCPT10PAT\_4\_SAS.rtf



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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 123)	123	98	75	54	33	19	15	7	3	0	0	0
TPC (N = 65)	65	36	13	6	2	2	0	0	0	0	0	0

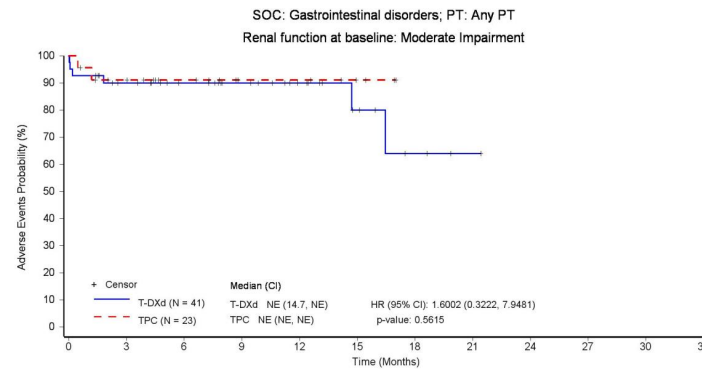
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 41)	41	31	25	19	13	7	3	1	0	0	0	0
TPC (N = 23)	23	18	11	6	6	3	0	0	0	0	0	0

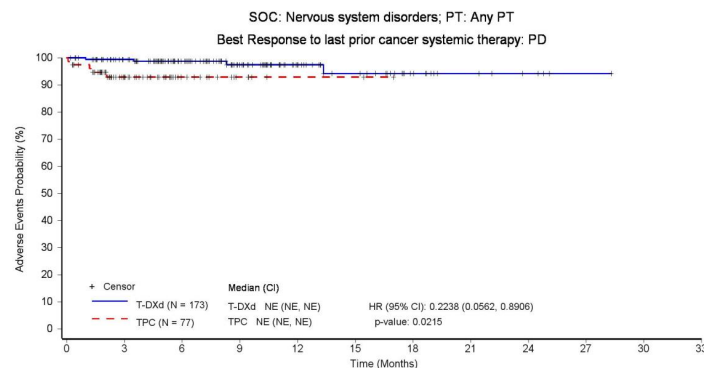
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 173)	173	144	102	69	39	27	14	7	4	1	0	0
TPC (N = 77)	77	41	16	6	2	2	0	0	0	0	0	0

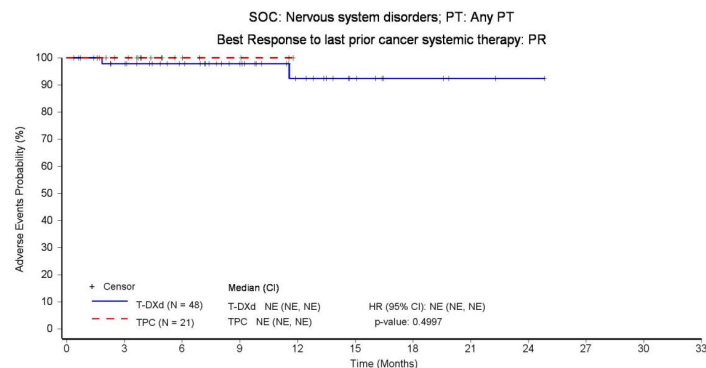
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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	T-DXd (N = 48)	TPC (N = 21)
0	48	21
3	43	14
6	35	5
9	26	3
12	15	0
15	8	0
18	4	0
21	2	0
24	1	0
27	0	0
30	0	0
33	0	0

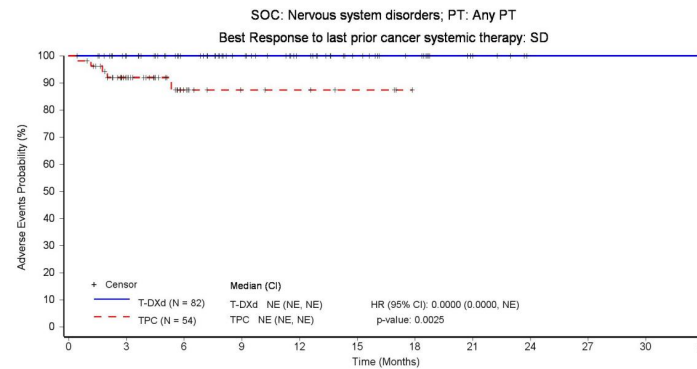
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 82)	82	67	53	41	31	21	15	5	1	1	1	0
TPC (N = 54)	54	33	13	6	5	3	0	0	0	0	0	0

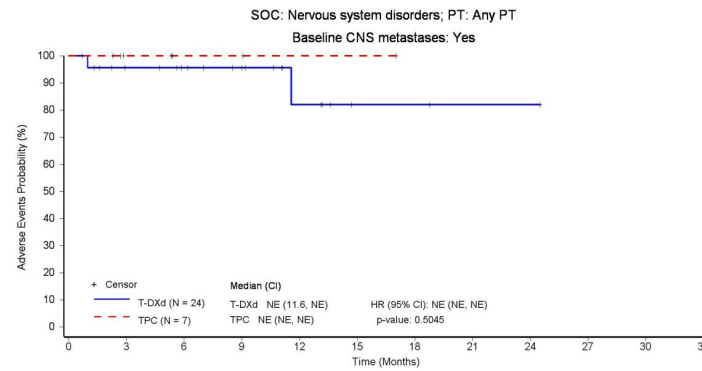
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 24)	24	18	15	12	6	2	2	1	1	0	0	0
TPC (N = 7)	7	4	2	2	1	1	0	0	0	0	0	0

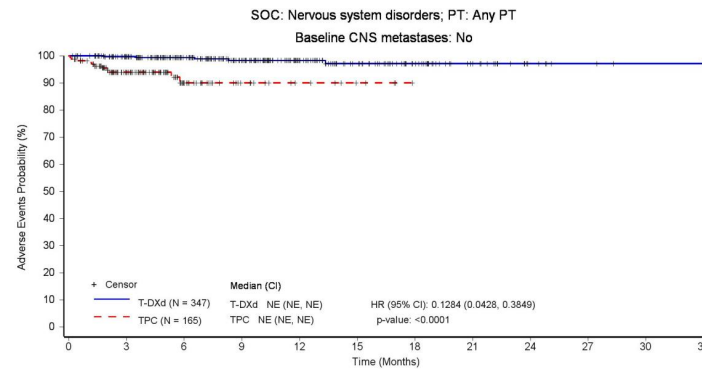
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

Time (Months)	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 347)	347	295	221	159	101	69	41	19	7	3	1	0
TPC (N = 165)	165	97	36	15	8	4	0	0	0	0	0	0

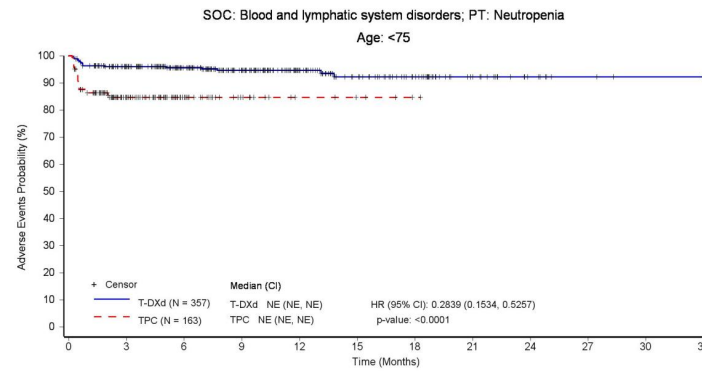
Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 357)	357	289	215	156	97	62	41	19	8	3	1	0
TPC (N = 163)	163	81	33	14	6	4	1	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

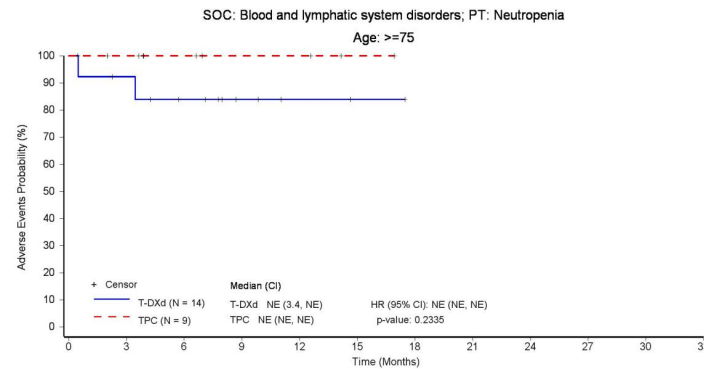
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DE.F.4.12.4 - Severe Treatment-emergent adverse events (NCI CTCAE grade  $\geq 3$ ) by system organ class (SOC) and preferred term (PT) observed for  $\geq 10$  patients in at least one arm and  $\geq 1\%$  of the patients in at least one arm - Kaplan-Meier plot - subgroup analysis - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set



Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
T-DXd (N = 14)	14	11	8	4	2	1	0	0	0	0	0	0
TPC (N = 9)	9	8	5	3	3	1	0	0	0	0	0	0

Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.13.1 - Treatment-emergent adverse events associated with discontinuation of study treatment by SOC and PT - Descriptive summary - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

MedDRA System Organ Class / Preferred Term	T-DXd (N=371)	TPC (N=172)
Subjects with any treatment-emergent adverse events associated with study drug discontinuation	60(16.2)	14(8.1)
Respiratory, thoracic and mediastinal disorders	41(11.1)	1(0.6)
Pneumonitis	21(5.7)	0
Interstitial lung disease	16(4.3)	0
Dyspnoea	2(0.5)	0
Pleural effusion	2(0.5)	0
Pulmonary embolism	0	1(0.6)

N: number of subjects in analysis set, n: number of subjects with events; %: proportion of number of subjects in analysis set

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:09; Program name: T4\_AEDISCSOCP1\_1\_SAS.sas; Output name: T4\_AEDISCSOCP1\_1\_SAS.rtf

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DE.T.4.13.1 - Treatment-emergent adverse events associated with discontinuation of study treatment by SOC and PT - Descriptive summary - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

MedDRA System Organ Class / Preferred Term	T-DXd (N=371)	TPC (N=172)
Investigations	6(1.6)	0
Ejection fraction decreased	2(0.5)	0
Blood bilirubin increased	1(0.3)	0
Electrocardiogram QT prolonged	1(0.3)	0
Lymphocyte count decreased	1(0.3)	0
Weight decreased	1(0.3)	0

N: number of subjects in analysis set, n: number of subjects with events; %: proportion of number of subjects in analysis set

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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DE.T.4.13.1 - Treatment-emergent adverse events associated with discontinuation of study treatment by SOC and PT - Descriptive summary - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

MedDRA System Organ Class / Preferred Term	T-DXd (N=371)	TPC (N=172)
Cardiac disorders	3(0.8)	1(0.6)
Cardiac failure	1(0.3)	0
Left atrial enlargement	1(0.3)	0
Stress cardiomyopathy	1(0.3)	0
Angina pectoris	0	1(0.6)

N: number of subjects in analysis set, n: number of subjects with events; %: proportion of number of subjects in analysis set

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
 Run date: 13SEP2022 – 17:09; Program name: T4\_AEDISCSOCP1\_1\_SAS.sas; Output name: T4\_AEDISCSOCP1\_1\_SAS.rtf

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DE.T.4.13.1 - Treatment-emergent adverse events associated with discontinuation of study treatment by SOC and PT - Descriptive summary - Destiny Breast 04 - DCO 11-Jan-2022 - safety analysis set

MedDRA System Organ Class / Preferred Term	T-DXd (N=371)	TPC (N=172)
Blood and lymphatic system disorders	2(0.5)	0
Disseminated intravascular coagulation	1(0.3)	0
Febrile neutropenia	1(0.3)	0
Gastrointestinal disorders	2(0.5)	3(1.7)
Colitis ischaemic	1(0.3)	0
Nausea	1(0.3)	0
Vomiting	1(0.3)	0
Abdominal pain upper	0	1(0.6)
Colitis	0	1(0.6)
Haemorrhoids	0	1(0.6)
Hepatobiliary disorders	2(0.5)	0
Hepatic failure	1(0.3)	0
Hyperbilirubinaemia	1(0.3)	0

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MedDRA System Organ Class / Preferred Term	T-DXd (N=371)	TPC (N=172)
Infections and infestations	2(0.5)	0
Pneumonia	1(0.3)	0
Staphylococcal bacteraemia	1(0.3)	0

N: number of subjects in analysis set, n: number of subjects with events; %: proportion of number of subjects in analysis set

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MedDRA System Organ Class / Preferred Term	T-DXd (N=371)	TPC (N=172)
General disorders and administration site conditions	1(0.3)	0
Fatigue	1(0.3)	0
Metabolism and nutrition disorders	1(0.3)	0
Hypokalaemia	1(0.3)	0

N: number of subjects in analysis set, n: number of subjects with events; %: proportion of number of subjects in analysis set

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MedDRA System Organ Class / Preferred Term	T-DXd (N=371)	TPC (N=172)
Eye disorders	0	1(0.6)
Ocular hypertension	0	1(0.6)
Nervous system disorders	0	6(3.5)
Neuropathy peripheral	0	1(0.6)
Peripheral sensory neuropathy	0	4(2.3)
Polyneuropathy	0	1(0.6)
Reproductive system and breast disorders	0	1(0.6)
Breast pain	0	1(0.6)
Skin and subcutaneous tissue disorders	0	1(0.6)
Palmar-plantar erythrodysesthesia syndrome	0	1(0.6)
Vascular disorders	0	1(0.6)
Superior vena cava occlusion	0	1(0.6)

N: number of subjects in analysis set, n: number of subjects with events; %: proportion of number of subjects in analysis set

Data source: DS8201-A-U303/restricted/rstrct\_eg/rstrct\_DCO\_20220111\_eg/rstrct\_eg\_valos/20220620\_heor\_AMNOG\_02/rstrct\_adam  
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